CAS# 97-74-5
Thiodicarbonic diamide ([(H2N)C(S)]2S), tetramethyl-

Molecular Formula: $C_6H_{12}N_2S_3$
Molecular Weight: 208.37

1.1 GENERAL SUBSTANCE INFORMATION

A. Type of Substance: Organic
B. Physical State: Yellow Solid
C. Purity: 95-98 % Typical for Commercial Products

1.2 SYNONYMS

Tetramethylthiuram Monosulfide
TMTM
Monothiurad®
Unads®
Perkacit® TMTM

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PHYSICAL-CHEMICAL DATA

*2.1 MELTING POINT

Value:	105 - 109.5° C
Decomposition:	No
Sublimation:	No
Method:	ASTM Standard Test Method D-1519
GLP:	Yes
Remarks:	Capillary Method for determining the initial and final melting point of organic compounds
Reference:	ASTM Standard Methods of Analysis
Reliability:	(1) Valid without restriction

*2.2 BOILING POINT

Value:	301.28° C
Pressure:	1 Atmosphere
Decomposition:	No data
Method:	Adapted Stein and Brown Method
GLP:	No
Remarks:	Calculation based on molecular structure and measured melting point value
Reference:	EPIWIN/MPBPWIN v1.40
Reliability:	(2) Valid with restrictions – modelling data

†2.3 DENSITY (relative density)

Type:	Density
Value:	1.38
Temperature: 20° C	
Method:	Other: Density of solids by displacement of liquid
GLP:	No
Remarks:	Density of solids by displacement in kerosene
Reference:	FF97.8-1 Flexsys Standard Methods of Analysis
Reliability:	(1) Valid without restriction

***2.4 VAPOUR PRESSURE**

Value:	2.7 x 10^{-4} mm Hg
Temperature: 25° C	
Method:	calculated
	Other: Modified Grain method
GLP:	No
Remarks:	Estimation method based on molecular structure and measured melting point value.
Reference:	EPIWIN/MPBPWIN v1.40
Reliability:	(2) Valid with restrictions – modelling data

***2.5 PARTITION COEFFICIENT $log_{10}P_{ow}$**

Log Pow:	0.75
Temperature: None	
Method:	calculated
	Other: SRC LogKow (KowWin) Program 1995
GLP:	No
Remarks:	Estimation method based on molecular structure fragments
Reference:	EPIWIN/KOWWIN v1.66
Reliability:	(2) Valid with restrictions – modelling data

***2.6 WATER SOLUBILITY**

A. Solubility

Value:	15 ppm
Temperature:	20° C
Method:	No data
GLP:	No data
Remarks:	Aqueous solutions prepared for antimicrobial experiments
Reference:	Murata, M., Sakabe, F. Nippon Nogei Kagaku Kaishi, 1961
Reliability:	(4) Not assignable – data from secondary literature source

B. pH Value, pKa Value

pH Value:	Not Applicable
pKa value	Not Applicable

2.11 OXIDISING PROPERTIES

†2.12 OXIDATION: REDUCTION POTENTIAL

2.13 ADDITIONAL DATA

A. Partition co-efficient between soil/sediment and water (Kd)

B. Other data – Henry's Law Constant

Results:	1.7 x 10^{-5} atm-m^3/mole
Remarks:	Calculated value from moist soil surfaces
Reference:	Environ Toxicol Chem 10: 1283-93 (1991)
	EPIWIN/HENRYWIN v3.10
Reliability:	(2) Valid with restrictions – modelling data

3. <u>ENVIRONMENTAL FATE AND PATHWAYS</u>

*3.1.1 PHOTODEGRADATION

Type:	Air
Light source:	Sunlight
Temperature:	25°C
Direct photolysis:	
Half life:	0.925 hours
Indirect Photolysis:	
Rate constant (radical):	138.7592 x 10^{-12} cm^3/molecule-sec
Method:	calculated Atmospheric Oxidation Program/SAR Methods, 1995
GLP:	No
Test substance:	Other: SAR
Remarks:	Rapid atmospheric degradation of test substance in vapor phase by reaction with photochemically produced hydroxyl radicals. Particulate phase test substance may be physically removed from air by both wet and dry deposition. If released to air, the test substance is expected to exist in both the vapor and particulate phases.
Reference:	Meylan, WH and Howard, PH, Chemosphere 26: 1193-99, 1999 EPIWIN/AOPWIN v1.90
Reliability:	(2) Valid with restrictions – modelling data

*3.1.2 STABILITY IN WATER

*3.2 MONITORING DATA (ENVIRONMENTAL)

3.3 TRANSPORT AND DISTRIBUTION BETWEEN ENVIRONMENTAL COMPARTMENTS INCLUDING ESTIMATED ENVIRONMENTAL CONCENTRATIONS AND DISTRIBUTION PATHWAYS

*3.3.1 TRANSPORT

Type:	Adsorption
Media:	Soil/Sediment
Method:	SRC Structure estimation method based on molecular connectivity indices, 1992
Results:	Koc = 10
Remarks:	The Koc value suggests that the test substance will have a very high mobility in soil and will not adsorb to suspended solids and sediment in water.
Reference:	EPIWIN/PCKOCWIN v1.66
Reliability:	(2) Valid with restrictions – modelling data

Type:	Volatility
Media:	Water
Method:	Estimation Method, 1990
Results:	Volatilization half-life from model river: 3 days Volatilization half-life from model lake: 28 days
Remarks:	Model river = 1 m deep flowing at 1 m/sec and wind velocity of 3 m/sec. Model lake = 1 m deep flowing at 0.05 m/sec and wind velocity of 0.5 m/sec.

Reference: Handbook of Chemical Property Estimation Methods, 1990
Reliability: (2) Valid with restrictions – modelling data

***3.3.2 THEORETICAL DISTRIBUTION (FUGACITY CALCULATION)**

Media: Air-biota-sediment-soil-water
Method: Fugacity level III
EPIWIN v3.10

Results:

	Mass Amount (%)	Half-life (hrs)	Emissions (kg/hr)
Air	0.266	1.85	1000
Water	56.3	900	1000
Soil	43.3	900	1000
Sediment	0.109	3600	0

Remarks: Persistence time estimated at 425 hours
Reference: EPISUITE/EPIWIN v3.10
Reliability: (2) Valid with restrictions – modelling data

***3.5 BIODEGRADATION**

3.6 BOD5, COD OR RATIO BOD5/COD

3.7 BIOACCUMULATION

Species: None
Exposure Period: Not Applicable
Temperature: Not Applicable
Concentration: Not Applicable
BCF: 2
Elimination: No
Method: Log Kow and regression-derived equation
Type of test: Other (Calculated)
GLP: No
Test substance: As specified in 1.1-1.4
Remarks: Calculated value compares favorably with measured values [1.1 to 4.4] of the structurally similar compound Tetramethylthiuram Disulfide [TMTD] in carp conducted by the Chemicals Inspection and Testing Institute in Japan.
Reference: Handbook of Chemical Property Estimation Methods, 1990
Reliability: (2) Valid with restrictions – modelling data

4. <u>ECOTOXICITY</u>

***4.1 ACUTE/PROLONGED TOXICITY TO FISH**

Type of test: Static
Closed system
Species: <u>Salmo gairdneri</u> (Rainbow Trout)
Exposure period: 96 hours
Results: LC_{50} (24h) >3.2 mg/l
LC_{50} (48h) = 3.2 mg/l
LC_{50} (96h) = 2.3 mg/l
NOEC = 0.18 mg/l

LOEC = 3.2 mg/l

Analytical monitoring: No

Method: EPA Methods for Acute Toxicity Tests with Fish, Macroinvertebrates and Amphibians, 1975

GLP: Yes

Test substance: As prescribed by 1.1-1.4, purity >95%

Remarks: Test fish were obtained from Spring Creek Hatchery in Lewistown, Montana. Test fish were held in culture tanks on a 16-hour daylight photoperiod and observed for at least 14 days prior to testing. A daily record of fish observations was maintained during the holding period, during which time the fish were fed a standard diet of commercial fish food until 48 hours prior to testing, when feeding was stopped. A 96-hour range-finding test preceded the definitive study. Test fish used had a mean weight of 1.1g and a mean standard length of 42 mm. The test was conducted in 5 gallon glass vessels containing 15 liters of ABC well water. The 0-hour measured control water parameters of this dilution water were dissolved oxygen 9.2 mg/l and pH 8.0. The test vessels were kept in a water bath at 12°C. Test fish were acclimated to the dilution water and test temperature, and held without food for 48 hours prior to testing. Nanograde Acetone was used to prepare the test solutions and as the solvent control. Fish were placed in the testing vessels within 20 minutes of the addition of the test material aliquots. All concentrations were observed once every 24 hours for mortality and abnormal effects. Dissolved oxygen values and pH ranges were monitored during the testing and remained within acceptable limits. As a quality check, test fish were challenged with Antimycin A. The estimated 96Hr LC50 and 95% confidence limits were within the 95% confidence limits reported in the literature, indicating that the fish were in good condition.

Reference: Monsanto AB-83-026 Analytical Bio-Chemistry Labs 07/23/83

Reliability: (1) Valid without restriction

Type of test: Static
Closed system

Species: Lepomis macrochirus (Bluegill Sunfish)

Exposure period: 96 hours

Results: LC_{50} (24h) = 4.4 mg/l
LC_{50} (48h) = 2.9 mg/l
LC_{50} (96h) = 2.6 mg/l
NOEC = 1.8mg/l
LOEC = 3.2 mg/l

Analytical monitoring: No

Method: EPA Methods for Acute Toxicity Tests with Fish, Macroinvertebrates and Amphibians, 1975

GLP: Yes

Test substance: As prescribed by 1.1-1.4, purity >95%

Remarks: Test fish were obtained from Osage Catfisheries in Osage Beach, Missouri. Test fish were held in culture tanks on a

16-hour daylight photoperiod and observed for at least 14 days prior to testing. A daily record of fish observations was maintained during the holding period, during which time the fish were fed a standard diet of commercial fish food until 48 hours prior to testing, when feeding was stopped. A 96-hour range-finding test preceded the definitive study. Test fish used had a mean weight of 0.11 g and a mean standard length of 18 mm. The test was conducted in 5 gallon glass vessels containing 15 liters of ABC well water. The 0-hour measured control water parameters of this dilution water were dissolved oxygen 7.8 mg/l and pH 7.9. The test vessels were kept in a water bath at 22°C. Test fish were acclimated to the dilution water and test temperature, and held without food for 48 hours prior to testing. Nanograde Acetone was used to prepare the test solutions and as the solvent control. Fish were placed in the testing vessels within 20 minutes of the addition of the test material aliquots. All concentrations were observed once every 24 hours for mortality and abnormal effects. Dissolved oxygen values and pH ranges were monitored during the testing and remained within acceptable limits. As a quality check, test fish were challenged with Antimycin A. The estimated 96Hr LC50 and 95% confidence limits were within the 95% confidence limits reported in the literature, indicating that the fish were in good condition.

Reference: Monsanto AB-83-025 Analytical Bio-Chemistry Labs 07/28/83

Reliability: (1) Valid without restriction

4.2 ACUTE TOXICITY TO AQUATIC INVERTEBRATES

***A. Daphnia**

Type of test: Static
Closed system

Species: Daphnia magna

Exposure period: 48 hours

Results: EC_{50} (24h) >3.2 mg/l
EC_{50} (48h) = 1.6 mg/l
NOEC < 1.0 mg/l

Analytical monitoring: No

Method: EPA Methods for Acute Toxicity Tests with Fish, Macroinvertebrates and Amphibians, 1975

GLP: Yes

Test substance: As prescribed by 1.1-1.4, purity >95%

Remarks: The Daphnia magna used in the test were cultured at the ABC facilities. The adult Daphnia were fed the algae Selenastrum capricornutum at lest every three days prior to testing and supplemented with a suspension of trout chow. The bioassay was conducted in 250 ml glass beakers containing 200 ml of ABC well water. Vessels were kept at 20°C in a temperature- controlled area. Lighting was maintained at 50-70 foot-candles on a 16-hour daylight photoperiod. An initial range-finding experiment was

	carried out to determine the exposure concentrations for the definitive test. Acetone was used as the solvent for the test solutions, and the experiment included both a control and a solvent control. Daphnia in all concentrations were observed once every 24 hours for mortality and abnormal effects. Dissolved oxygen levels and pH were monitored throughout the testing and were considered adequate and equivalent to those measurements in the control chamber. All concentrations of the test substance demonstrated at least abnormal effects after 48 hours, so a definitive no-effect level could not be determined.
Reference:	Monsanto AB-83-027 Analytical Bio-Chemistry Labs 07/07/83
Reliability:	(1) Valid without restriction

***4.3 TOXICITY TO AQUATIC PLANTS, e.g. algae**

Species:	*Chorella pyrenoidosa* (Green algae)
Endpoint:	Biomass
Exposure period:	96 hours
Results:	EC_{50} 96hr = 1.0 mg/l
Analytical monitoring:	No
Method:	OECD 201, Algae, Growth Inhibition Test, 1984 Closed system
GLP:	Yes
Test substance:	As prescribed by 1.1-1.4, purity >95%
Remarks:	Thiurams are generally recognized as being toxic to aquatic plants. EC50 value compares favorably to those of the structurally similar compounds TETD (1.8 mg/l) and TMTD (1.0 mg/l)
Reference:	Van Leeuwen, C.J., Rijskwaterstaat Communications 44, 1986
Reliability:	(1) Valid without restriction

5. TOXICITY

***5.1 ACUTE TOXICITY**

5.1.1 ACUTE ORAL TOXICITY

Type:	LD_{50}
Species/strain:	Rats, Sprague-Dawley Albino
Value:	1320 mg/kg bw Discriminating dose: 1580 mg/kg bw
Sex:	Male/female
# of Animals:	25
Vehicle:	Corn Oil
Doses:	794, 1000, 1260, 1580 and 2000 mg/kg bw
Method:	Other: Defined Lethal Dose, 1973
GLP:	No data
Test substance:	As prescribed by 1.1-1.4, purity >95%
Remarks:	Twenty five albino rats were randomly divided into five groups consisting of five animals, both male and female.

Body weight ranges for the test animals was 220-235 g for males and 210-235 for females. The test animals were administered a single dose of the test substance in a 25% suspension in corn oil via oral gavage. Dosage levels were 794, 1000, 1260, 1580 and 2000 mg/kg bw. Initial signs of intoxication were reduced appetite and activity (one to four days in survivors), followed by increasing weakness, collapse and death. Time of mortality was 1-7 days, with most deaths occurring within four days.

Results:

Dose mg/kg	Mortalities-Male	Mortalities-Female	Combined
794	0/3	1/2	1/5
1000	0/ 2	2/3	2/5
1260	0/3	2/2	2/5
1580	1/2	2/3	3/5
2000	3/3	2/2	5/5

Gross autopsy findings on the decedents showed lung hyperaemia, slight liver discoloration and gastrointestinal inflammation. Following a 10-day recovery period, the survivors were sacrificed and autopsied. All viscera appeared normal in these animals.

Reference: Monsanto Y-73-192 Younger Laboratories, 11/16/73

Reliability: (2) Valid with restrictions – age of study, lack of method details

5.1.2 ACUTE INHALATION TOXICITY

5.1.3 ACUTE DERMAL TOXICITY

Type: LD_{50}
Species/strain: Rabbits, New Zealand Albino
Sex: Male/female
# of Animals: 4
Vehicle: Corn Oil
Doses: 1260, 2000, 3160 and 5010 mg/kg bw
Exposure Time: 24 Hours
Value: >2000 mg/kg bw
Method: Other: Defined Lethal Dose, 1973
GLP: No data
Test substance: As prescribed by 1.1-1.4, purity >95%
Remarks: Four rabbits, both male and female, were randomly assigned to four dosage groups. Each animal was exposed for a period of 24 hours to the test substance as a 40% suspension on corn oil as a single application to a shaved skin area. Dose levels were 1260, 2000, 3160 and 5010 mg/kg bw. Initial signs of intoxication included reduced appetite and activity (five to twelve days in survivors), followed by increasing weakness, collapse and death. There were no mortalities at the two lowest dose levels. Mortality occurred on Day 14 at the 3160 dose level, and on Day 9 at the 5010 dosage. Findings from the gross autopsy on decedents included lung congestion, enlarged liver with hyperemia, enlarged gall bladder, kidney discoloration and

gastrointestinal inflammation. After 14 days, the survivors were sacrificed and autopsied. All viscera appeared normal in these animals.

Reference: Monsanto Y-73-192 Younger Laboratories, 11/16/73

Reliability: (2) Valid with restrictions – age of study, lack of method details

5.2 CORROSIVENESS/IRRITATION

5.2.1 SKIN IRRITATION/CORROSION

Species/Strain: Rabbits, New Zealand Albino
Sex: Male/female
# of Animals: 6
Exposure time: 24 hours
Results: Slightly irritating
Classification: Not irritating
Method: F.H.S.A. Modified Draize, 1973
GLP: No data
Test substance: As prescribed by 1.1-1.4, purity >95%
Remarks: 100 mg of the test substance was applied to the eyes of six albino rabbits. The cornea, iris and conjunctivae of each animal were examined and scored on a scale of 1-10 immediately after application, after 10 minutes, after 1 hour, and after 24, 48 72 and 168 hours after application.
Immediate: Slight discomfort
10 min: Slight to moderate erythema, copious discharge
1 hr: Moderate erythema, copious discharge
24 hr: mean score 8.6, slight to moderate erythema, copious discharge
48 hr: mean score 3.6, slight erythema and discharge
72 hr: all scored 0
168 hr: all scored 0
Reference: Monsanto Y-73-192 Younger Laboratories 1973
Reliability: (2) Valid with restrictions - age of study, lack of method details

5.2.2 EYE IRRITATION/CORROSION

Species/strain: Rabbits, New Zealand Albino
Results: Slightly irritating
Classification: Not irritating
Method: F.H.S.A. Modified Draize 1973
GLP: No data
Test substance: As prescribed in 1.1-1.4, purity >95%
Remarks: 0.5 grams of the test substance as a finely ground powder was applied to the shaved skin of six albino rabbits for 24 hours. The animals were examined and the skin graded on a scale of 0-8 for erythema and edema at 4, 24, 48, 72 and 168 hours. Mean score for erythema at 24 and 72 hours was 0.7. All animals scored 0 for edema throughout the test.
Reference: Monsanto Y-73-192 Younger Laboratories 1973

Reliability: (2) Valid with restrictions - age of study, lack of method details

*5.4 REPEATED DOSE TOXICITY

Species/strain: Rats, Wistar
Sex: Male/Female
Route of Administration: Aqueous gavage
Exposure period: 4 Weeks
Frequency of treatment: 5 consecutive days/week
Post exposure observation period: No data
Dose: 0, 26, 520 or 867 mg/kg bw
Control group: Yes , concurrent vehicle
NOEL: Not Determined
LOEL: 26 mg/kg bw
Results: The test substance was administered to groups of male and female rats for 5 days/week for four weeks in aqueous gavage solutions. Red blood cell counts and hemoglobin levels were significantly lower in the 26 mg/kg group. Other clinical chemistry parameters were unchanged. Body weights and food consumption were also reduced in this group. Consumption of drinking water was increased. No change in hepatic microsomal enzyme activities was noted. In limited pathology examinations, no changes were seen in lungs, heart, spleen, muscle, brain or sciatic nerves. Mild, generalized swelling of liver cells and renal tubular epithelia were reported as minor organ changes. Radiolabeled palmitic acid incorporated into the phospholipids of the endoplasmic reticulum was reduced. The authors concluded that microsomal hydroxylase enzyme system was sensitive to inhibition by the test substance.
Method: No data
GLP: No data
Test substance: .As prescribed by 1.1-1.4, purity: Commercial grade
Reference: Environmental Research 28, 199-221 (1982)
Reliability: (2) Valid with restrictions – lack of method detail

Species/strain: Rats, strain not specified
Sex: Male/Female
Route of Administration: Inhalation (dust)
Exposure period: 15 Days
Frequency of treatment: 2 hours/day
Post exposure observation period: No data
Dose: 400 mg/m3
Control group: Yes, concurrent no treatment
NOEL: Not Determined
LOEL: Not Determined
Results: Male and female rats were exposed to the test substance as a fine dust for 2 hours/day for 15 consecutive days. There were no mortalities reported during the studies. Treated animals exhibited reduced weight gain and food consumption compared to controls. Findings from gross necropsy examinations were degenerative changes in the liver and kidneys of the treated animals.

Method: No data
GLP: No data
Test substance: As prescribed by 1.1-1.4, purity >95%
Reference: Soviet Rubber Technology 36, 1964
Reliability: (2) Valid with restrictions – lack of method details

***5.5 GENETIC TOXICITY IN VITRO**

A. BACTERIAL TEST

Type: Ames Test (Bacterial Reverse Mutation)
System of testing: Salmonella typhimurium TA-1535, TA-1537, TA-1538, TA-98, TA-100
Saccharomyces cerevisiae D4
Concentration: Without Activation: 0.1, 1.0, 10, 100 and 500 µg/plate
With Activation: 0.1, 1.0, 10, 100 and 500 µg/plate
Metabolic activation: With and without
Results:
Cytotoxicity conc: With metabolic activation: 500 µg [10 µg for TA-98]
Without metabolic activation: 500 µg [10 µg for TA-98]
Precipitation conc: No data
Genotoxic effects:
With metabolic activation: Positive for TA-1535 only
Without metabolic activation: Negative
Method: EPA/OPPTS 870.5265, 1976
GLP: No data
Test substance: As prescribed in 1.1-1.4, purity >95%
Remarks: The test compound was evaluated for genetic activity in microbial assays with and without the addition of mammalian metabolic activation preparations. The activation system used was S-9 homogenate from Aroclor 1254-induced adult male Sprague-Dawley rat livers. Either DMSO or DI water was used to prepare the stock solutions of all solid materials. Chemicals used as positive controls for the non-activation assays were Methylnitrosoguanidine (MNNG), 2-Nitrofluorene (NF) and Quinacrine mustard (QM). Positive control chemicals used for the activation assays were 2-Anthramine (ANTH), 2-Acetylaminofluorine (AAF) and 8-Aminoquinoline (AMQ). The compound was tested over a series of concentrations such that there was either quantitative or qualitative evidence of some chemically induced physiological effects at the high dose level. The low dose in all cases was below a concentration that exhibited any toxic effect.
Non-activation results: No mutagenic activity in any indicator organism at any dose.
Activation results: Strain TA-1535 exhibited mutagenic response at the three highest dose levels (10, 100, 500 µg/plate). All other tester strains did not exhibit mutagenic activity at any dose level.
Reference: Monsanto BIO-76-275 Litton Bionetics, 12/30/76
Reliability: (1) Valid without restrictions

B. NON-BACTERIAL IN VITRO TEST

Type: Mouse Lymphoma Forward Mutation Assay
System of testing: L5178Y
Concentration: 2.5 – 5.0 µg/ml
Metabolic activation: With and without
Results:
Cytotoxicity conc: With metabolic activation: 5 µg/ml
Without metabolic activation: 10 µg/ml
Precipitation conc: 320 µg/ml
Genotoxic effects:
With metabolic activation: Negative
Without metabolic activation: Negative
Method: Other: Clive, D. and Spector, J.F.S. (1975) Mutation Res. 31, 17-29
GLP: No data
Test substance: As prescribed in 1.1-1.4, purity >95%
Remarks: The test substance was dissolved in DMSO at 250 µg/ml. Working solutions were made of this stock solution by making a series of two-fold serial dilutions with DMSO. One tenth ml of each stock solution or one of the working dilutions was added to 3x10(6) cells in 10 ml of medium to achieve the desired final concentration. A yellow precipitate formed when the solutions were added to culture medium at final concentrations of 320 µg/ml or greater. The test substance was toxicity tested over the range of 5 µg/ml to 2.5 µg/ml. Concentrations greater than 10 µg/ml proved to be highly cytotoxic in the absence of an activation system and even more toxic in the presence of a mouse liver S-9 preparation. DMSO (1%) was used as the solvent control substance. Growth medium without the addition of solvent was used as a negative control. No genetic effects were attributed to the presence of the solvent. EMS and DMN were used as reference mutagens and induced mutation frequencies within the expected range.

Non-Activation

	Conc.	Mutant clones	Viable clones	Mutant frequency x10(-6)
Solvent Control	---	52.5	282	18.0
Negative Control	---	110.0	342.0	32.5
EMS	0.5 µl/ml	339.0	132.0	256.8
TMTM	2.5 µg/ml	67.0	305.0	22.0
	5.0 µg/ml	92.0	267.0	34.5
	10.0 µg/ml	7.0	485.0	1.4
	20.0 µg/ml	10.0	273.0	3.7

Activation with S-9

	Conc.	Mutant clones	Viable clones	Mutant frequency x10(-6)
Solvent Control	---	34.0	316.0	10.0
Negative Control	---	75.0	555.1	13.6
DMN	0.3 µl/ml	360.0	67.0	537.3
TMTM	0.02 µg/ml	41.0	166.0	24.7
	0.04 µg/ml	111.0	374.0	29.7
	0.08 µg/ml	64.0	258.0	24.8
	0.16 µg/ml	37.0	376.0	9.8
	0.32 µg/ml	62.0	280.0	22.1

The test substance was considered to be not active in the L5178Y
Mouse Lymphoma Assay.

Reference: Monsanto BIO-77-323 Litton Bionetics, 07/78
Reliability: (1) Valid without restriction

***5.6 GENETIC TOXICITY IN VIVO**

Type: *In Vivo* Bone Marrow Cytogenetics
Species/strain: Rats, Sprague-Dawley
Sex: Male/Female
Route of Administration: Oral gavage, single dose
Exposure period: Sacrifice at 6, 24 and 48 hours after dosing
Doses: 750 mg/kg bw for females and 1300 mg/kg bw for males
Results:
Effect on mitotic index or P/N ratio:
Mitotic index depression: 24% at 6 hours
33% at 24 hours
56% at 48 hours
Genotoxic effects: Negative
Method: OECD 475 (1983)
GLP: Yes
Test substance: As prescribed in 1.1-1.4, purity 95.5% by UV/VIS
Remarks: Two toxicity range finding experiments were performed to determine the doses for the definitive experiment. Dose of 1300 mg/kg bw of TMTM for males represented 43% of the LD50, and dose of 750 mg/kg bw TMTM represented 75% of the LD50 for females. Control groups received either 10 ml/kg bw of vehicle control (corn oil), or 40 mg/kg bw of the positive control cyclophosphamide. Bone marrow was sampled at 6, 24 and 48 hours after dosing with the vehicle or the test substance TMTM. A single sampling time of +24 hours was used for the positive control group. Slides were scored for increases in the proportion of aberrant metaphases and in the frequency of aberrations/cell. In the main cytogenetic experiment, the test substance TMTM was toxic to male and female rats as evidenced by clinical signs of toxicity (hypoactivity). Statistically significant decreases in mean body weight were observed for the TMTM-treated male and female rats at +24 and +48 hours,

and in the positive control-treated male rats at +24 hours. No statistically significant increases in the proportion of aberrant cells or aberrations/cell were observed at the 6, 24 and 48 hour time points. Significant induction of toxicity, measured as mitotic index depression, was observed at the 6 hour (24%), 24 hour (33%), and 48 hour (56%) time points. The positive control group (cyclophosphamide) yielded the expected positive responses, indicating the adequacy of the experimental test conditions for the detection of clastogens.
The test substance, TMTM, was judged to be non-clastogenic under the experimental conditions.

Reference: Monsanto ML-89-512 Monsanto/Pharmakon 1992
Reliability: (1) Valid without restriction

5.7 CARCINOGENICITY

Species/strain: Mice, B6C3F1 and B6AKF1
Sex: Male/Female
Route of Administration: Oral gavage on days 7-28, oral feed for remainder
Single subcutaneous injection on Day 28
Exposure period: 18 months
Frequency of treatment: Daily for one study, once for other study
Post-exposure observation: Not determined
Doses: Gavage = 100 mg/kg bw (Feed = 377 ppm)
Injection = 0.05 ml of suspension
Control group: Yes
Other: Positive Control
Results: In a National Cancer Institute study, 18 virgin male and 18 virgin female mice from two hybrid strains were dosed with the test substance. Two types of studies were run simultaneously. One group of 36 mice received a single subcutaneous injection administered in the nape of the neck at the 28^{th} day of age, with no exposure to the test substance thereafter. The second group of 26 mice received a daily oral gavage dose of the test article administered from the 7^{th} to 28^{th} days of age, and then daily in their feed mix thereafter. All compounds administered orally as positive controls were carcinogenic, while only two of the positive controls (urethane, ethyleneimine) administered subcutaneously had carcinogenic activity. There were no findings of carcinogenic effects attributed to the test substance in either 18-month study.
Method: Litton Bionetics Research Labs Protocol
GLP: No data
Test substance: As prescribed by 1.1-1.4, purity >97%
Remarks: Study was undertaken to determine the carcinogenic potential of 130 chemicals that had been used in the formulations of insecticides, herbicides and fungicides.
Reference: Litton Bionetics/NCI Report # PB223-159 (1968)
Reliability: (2) Valid with restrictions. Intubation/feed part of this study followed generally accepted parameters for a 1968 carcinogenicity assessment, but not all test parameters comply with current guidelines. No GLP data. The

reliance on a single subcutaneous injection as adequate for the other portion of this study is questionable.

***5.8 TOXICITY TO REPRODUCTION**

***5.9 DEVELOPMENTAL TOXICITY/ TERATOGENICITY**

Species/strain: Mice, B6C3F1, BL6 and B6AKF1
Sex: Female
Route of Administration: Subcutaneous
Duration of the test: 18 days
Exposure period: Day 6-14 of gestation
Frequency of treatment: Daily
Doses: 46.4 and 100 mg/kg bw
Control group: Yes
Other: Positive Control
NOEL Maternal Toxicity: >100 mg/kg
NOEL teratogenicity : >100 mg/kg
Results: Groups of pregnant mice were treated with the test substance via subcutaneous injections into the nape of the neck to evaluate the effect on implantation, foetal mortality, weight and development, placental weight, amniotic fluid volume, maternal weight, and maternal liver/body weight ratio. A Positive Control of 2,4,5-T was used. All treated mice were sacrificed on Day 18 of gestation. In the postnatal study, neonates were examined at birth, at 8 days, and then sacrificed. There were no embryotoxic or teratogenic effects observed that were attributed to the test substance in any strain of mice.
Maternal general toxicity: No toxic effects observed
Pregnancy/litter data: No toxic effects observed
Foetal data: No foetal anomalies observed
Method: Litton Bionetics Research Labs Protocol
GLP: No data
Test substance: As prescribed by 1.1-1.4, purity >97%
Remarks: The test substance was one of 48 compounds evaluated in this experiment. All compounds were selected due to use as insecticides, herbicides or fungicides.
Reference: NTIS PB223-160
Reliability: (2) Valid with restrictions. Well documented and scientifically acceptable, but not all test parameters in compliance with current guidelines. No GLP data.

5.10 OTHER RELEVANT INFORMATION

A. Specific toxicities

Type: Skin Sensitisation / Human Skin Patch Test
Results: Patch testing on 50 human volunteers with the rubber accelerator TMTM produced 1 positive reaction on initial application, 7 positive reactions during the course of 15 serial applications, and 5 positive reactions on a subsequent rechallenge. It was concluded that the test

	substance was a cumulative irritant as well as a sensitising agent.
Remarks:	Method used was the Shelanski and Shelanski Repeated Insult Patch Test.
Reference:	Monsanto SH-76-3 Product Investigations, Inc. 1976
Reliability:	(2) valid with restrictions – age of study

Type:	Skin Sensitisation / Human Skin Patch Test
Results:	Patch testing was carried out on 128 patients who had experienced type IV allergic reactions due to rubber products. 85 out of 128 patients reacted positively to tetramethylthiuram monosulfide.
Remarks:	Patients were tested with the standard “thiuram mix”, and then to individual thiuram-type compounds that are components of that mix. Rubber articles implicated in this study included rubber boots, rubber aprons, rubber coats, rubber gloves, rubber shoes, and the elastic in underwear.
Reference:	Contact Dermatitis 10 (4): 125 (1984)
Reliability:	(2) Valid with restrictions – lack of test method details

B. Toxicodynamics, toxicokinetics

*** 5.11 EXPERIENCE WITH HUMAN EXPOSURE**

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25. NTIS PB-223-159 Evaluation of Carcinogenic, Teratogenic and Mutagenic Activities of Selected Pesticides and Industrial Chemicals, Litton Bionetics/National Cancer Institute, USA 401 pages, August, 1968
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CAS# 97-77-8
Disulfiram

Molecular Formula: **C10H20N2S4**
Molecular Weight: 296.66

1. General Information

1.1 General Substance Information

Substance type: organic
Physical status: solid

1.2 Synonyms

1,1'-dithiobis(N,N-diethylthioformamide)
Source: Akzo Nobel Chemicals b.v. Amersfoort

antabus
Source: Akzo Nobel Chemicals b.v. Amersfoort

disulfiram
Source: Akzo Nobel Chemicals b.v. Amersfoort

ethyl thiram
Source: Akzo Nobel Chemicals b.v. Amersfoort

ethyl thiurad
Source: Akzo Nobel Chemicals b.v. Amersfoort

TETD
Source: Akzo Nobel Chemicals b.v. Amersfoort

tetraethylthiuram disulfide
Source: Akzo Nobel Chemicals b.v. Amersfoort

1.3 Impurities

1.4 Additives

2. Physico-chemical Data

2.1 Melting Point

Value: 71.5°C
Source: CRC Handbook of Chemistry and Physics, 76th ed. 1996
Reliability: (1) Valid without restriction - accepted literature source

Value: Initial melt 64°C
Final melt 69-73°C
Method: Flexsys Standard Methods of Analysis FF 83.9, 1996
Source: Flexsys America L.P.
Reliability: (1) Valid without restriction
(2)

2.2 Boiling Point

Value: 117°C
Pressure: 22.6647 hPa
Remark: (17 mm Hg)
Source: CRC Handbook of Chemistry and Physics, 76th ed. 1996
Reliability: (1) Valid without restriction – accepted literature source
(1)

2.3 Density

Type: density
Value: 1310 kg/m3 at 20 degree C
Source: Akzo Nobel Chemicals b.v. Amersfoort
Reliability: (1) Valid without restriction
(3)

Type: bulk density
Value: 340 - 380 kg/m3
Source: Akzo Nobel Chemicals b.v. Amersfoort
Reliability: (1) Valid without restriction
(3)

2.4 Vapour Pressure

Value: 6.61E-006 at 1013 hPa
Method: MPBPWIN v1.40, Modified Grain Method
Remark: Calculation based on molecular structure and measured Melting point, water solubility and Log Kow
Source: EPIWIN MPBPWIN v1.40
Reliability: (2) Valid with restrictions –modeling data
(4)

2.5 Partition Coefficient

Value: 3.88
Method: No data
Source: Hansch, C. et al, 1995
Reliability: (1) valid without restriction – accepted literature source
(5)

2.6.1 Water Solubility

Value: 4.09 mg/l
Temperature: 25°C
Source: Yalowsky and Dannenfelser, The AQUASOL database of Aqueous Solubility, 5th edition, 1992
Reliability: (1) valid without restriction – accepted literature source
(6)

Value: 0.02 g/100 ml
Temperature: 25°C
Source: Monsanto MSDS for Ethyl Thiurad, 1983; The Merck Index, 1996
Reliability: (1) valid without restriction – accepted literature source
(7)

2.7 Flash Point

Value:	>120°C
Method:	ASTM D 56-96, Test Method for Flash Point by Tag Closed Tester, 1956 (Revised 1996)
Source:	Monsanto MSDS for Ethyl Thiurad, 1983
Reliability:	(1) Valid without restriction

(8)

2.12 Additional Remarks

Remark:	The chemical forms chelates with certain metals, eg. Fe and Cu.
Source:	Akzo Nobel Chemicals b.v. Amersfoort

(9)

3. Environmental Fate and Pathways

3.1.1 Photodegradation

Type:	air
INDIRECT PHOTOLYSIS	
Sensitizer:	OH
Conc. of sens.	1560000 molecule/cm3
Rate constant:	392.4139 E-12 cm3/(molecule-sec)
Degradation:	50 % after 19.625 minutes
Method:	other (calculated): AOP Program (v1.89)
Year:	1999
GLP:	No
Test substance:	other TS: molecular structure and measured Melting point, water solubility and Log Kow
Reference:	EPIWIN/AOPWIN v1.90
Reliability:	(2) Valid with restrictions - Accepted calculation

(10)

3.1.2 Stability in Water

Type:	Hydrolysis
Method:	
Year:	GLP:
Test substance:	Other
Remark:	If released in water TETD is expected to hydrolyze at a rate similar to that of its analog TMTD whose half-life is 2 days at pH7. In more alkline water at pH 9, hydrolysis will occur much faster, with a half-life of 4 to 7 hours.
Source:	Akzo Nobel Chemicals b.v. Amersfoort
Reliability:	(2) Valid with restrictions: data from a structurally similar compound and general class of compounds which have been extensively tested for environmental effects

(9)

3.1.3 Stability in Soil

Type:	Radiolabel:
Concentration:	
Cation exch. capac.	
Microbial biomass:	
Method:	
Year:	GLP:

Test substance:
Remark: As for the analog of TMTD, TETD has a relatively short half-life in soil and no apparent leaching potential. The half-life of TMTD in soil was measured to be approx. 43 days. It may photodegrade on the soil surface. In moist soil hydrolysis may occur (see 3.1.2).
Source: Akzo Nobel Chemicals b.v. Amersfoort
Reliability: (2) Valid with restrictions: data from a structurally similar compound and general class of compounds which have been extensively tested for environmental effects

(9)

3.3.1 Transport between Environmental Compartments

Type: Adsorption
Media: Soil/Sediment
Method: SRC Structure estimation method based on molecular connectivity indices, 1992
Results: Koc = 92.67; Log Koc = 1.967
Remarks: Estimation based on molecular structure and measured melting point, water solubility and Log Kow
Reference: EPIWIN/PCKOCWIN v1.66
Reliability: (2) Valid with restrictions – Modelling data

(11)

Type: Volatility
Media: Water
Method: Estimation Method, 1990
Results: Volatilization half-life from model river: 1856 hours
Volatilization half-life from model lake: 2.034E+004 hours
Remarks: Model river = 1 m deep flowing at 1 m/sec and wind velocity of 3 m/sec.
Model lake = 1 m deep flowing at 0.05 m/sec and wind velocity of 0.5 m/sec.
Reference: Handbook of Chemical Property Estimation Methods, 1990
Reliability: (2) Valid with restrictions – Peer-reviewed published data from a generally accepted and validated estimation method

(12)

Media: Air-biota-sediment-soil-water
Method: Fugacity level III
EPIWIN v3.10
Results:

	Mass Amount (%)	Half-life (hrs)	Emissions (kg/hr)
Air	0.0678	0.654	1000
Water	23.7	900	000
Soil	73.7	900	1000
Sediment	2.52	3.6E+003	0

Remarks: Persistence time = 582 hours
Calculation based on molecular structure and measured melting point, water solubility and Log Kow
Reference: EPISUITE/EPIWIN v3.10
Reliability: (2) Valid with restrictions – Modelling data

(13)

3.3.2 Distribution

3.4 Mode of Degradation in Actual Use

3.5 Biodegradation

Type:
Inoculum:
Method:
  Year: GLP:
Test substance:
Remark: Like its analog tetramethylthiuram disulfide (TMTD), tetraethylthiuram disulfide is expected to be readily biodegradable. TMTD is completely mineralized in 28 days in a Closed Bottle Test.
Source: Akzo Nobel Chemicals b.v. Amersfoort
Reliability: (2) Valid with restrictions: data from a structurally similar compound and general class of compounds which have been extensively tested for environmental effects
14)

3.6 BOD5, COD or BOD5/COD Ratio

3.7 Bioaccumulation

Species: Salmo gairdneri
Exposure period: at 25 degree C
Concentration: no data
BCF: 225
Elimination: no data
Method: other: not specified
  Year: 1986 GLP: no data
Test substance: As prescribed by 1.1-1.4, purity: 98%
Remark: Measured value
Source: Van Leeuwen, C.J., 1986
Reliability: (4) Unassignable - data from a secondary literature source
(15)

Species: Other
BCF: 193.9
Method: other: BCFWIN v2.14
  Year: 2000 GLP: no
Test substance: As prescribed by 1.1-1.4, purity: 98%
Remark: Calculation method based on molecular structure and measured water solubility, Log Kow and melting point. Good agreement with measured BCF in trout
Source: EPIWIN/BCFWIN, 2000
Reliability: (2) Valid with restrictions - modeling data
(16)

4. Ecotoxicity

AQUATIC ORGANISMS

4.1 Acute/Prolonged Toxicity to Fish

Type: static
Species: Lepomis macrochirus(Fish, fresh water)
Exposure period: 96 hours
Unit: mg/l Analytical monitoring: no
Method: EPA-660/3-75-009, Methods for Acute Toxicity Tests with Fish, Macroinvertebrates and Amphibians
Year: 1975 GLP: Yes

Test substance: As prescribed by 1.1-1.4, purity: 98%
LC50 (24 hr): 0.075 mg/l
LC50 (48 hr): 0.071 mg/l
LC50 (96 hr): 0.067 mg/l
LOEC: 0.018 mg/l
NOEC: 0.010 mg/l
Concentrations: 0, 0.010, 0.018, 0.032, 0.056 and 0.10 mg/l
Remark: The acute toxicity of TETD to bluegill sunfish was assessed using the methods outlined by the USEPA Committee on Methods for Toxicity Tests with Aquatic Organisms. There were no deviations from this protocol. Water quality parameters of temperature, dissolved oxygen and pH were measured throughout the test and remained within acceptable limits. As a quality check, the test fish were challenged with the reference compound Antimycin A, indicating that the fish were in good condition. Ten fish, mean standard weight 0.13 grams and mean standard length 19 mm, were used in each test concentration and controls. A 96-hour range-finding study preceded the definitive test. Nanograde acetone was used as the test compound solvent and as the solvent control. Test fish were placed in the test aquaria within 20 minutes after addition of the test compound aliquots. All concentrations were observed once every 24 hours for mortality and abnormal effects. Statistical analysis of the concentration/effect data was obtained using a computerized LC50 program developed by Stephan et al. This program calculated the LC50 statistic and 95% confidence limits using the binomial, the moving average and the probit tests.
Source: Monsanto ABC 31078, 1983
Reliability: (1) Valid without restriction

(17)

Type: static
Species: Salmo gairdneri(Fish, fresh water)
Exposure period: 96 hours
Unit: mg/l Analytical monitoring: no
Method: EPA-660/3-75-009, Methods for Acute Toxicity Tests with Fish, Macroinvertebrates and Amphibians
Year: 1975 GLP: Yes
Test substance: As prescribed by 1.1-1.4, purity: 98%
LC50 (24 hr): 0.27 mg/l
LC50 (48 hr): 0.22 mg/l
LC50 (96 hr): 0.22 mg/l
LOEC: 0.056 mg/l
NOEC: <0.056 mg/l
Concentrations: 0, 0.056, 0.10, 0.18, 0.32 and 0.56 mg/l
Remark: The acute toxicity of TETD to rainbow trout was assessed using the methods outlined by the USEPA Committee on Methods for Toxicity Tests with Aquatic Organisms. There were no deviations from this protocol. Water quality parameters of temperature, dissolved oxygen and pH were measured throughout the test and remained within acceptable limits. As a quality check, the test fish were challenged with the reference compound Antimycin A, indicating that the fish were in good condition. Ten fish, mean standard weight 0.90 grams and mean standard length 38 mm, were used in each test concentration and controls. A 96-hour range-finding study preceded the definitive test. Nanograde acetone was used as the test compound solvent and as the solvent control. Test fish were placed in the test aquaria within 20 minutes after addition of the test compound aliquots. All concentrations were observed once every 24 hours for mortality and abnormal

effects. Statistical analysis of the concentration/effect data was obtained using a computerized LC50 program developed by Stephan et al. This program calculated the LC50 statistic and 95% confidence limits using the binomial, the moving average and the probit tests.
Source: Monsanto ABC 31079, 1983
Reliability: (1) Valid without restriction

(18)

Type: semistatic
Species: Brachydanio rerio (Fish, fresh water)
Exposure period: 10 day
Unit: µg/l Analytical monitoring: no
Method: OECD Guide-line 204 "Fish, Prolonged Toxicity Test: 14-day Study"
Year: GLP: no data
Test substance: as prescribed by 1.1 - 1.4
Remark: Renewal of the test media after 2 days.
Results: NOEC survival: 3.2 ug/l
NOEC hatching: 3.2 ug/l
NOEC malformations: < 10 ug/l
Source: Akzo Nobel Chemicals b.v. Amersfoort
Reliability: (1) Valid without restriction. Guideline study

(19)

Type: semistatic
Species: Poecilia reticulata (Fish, fresh water)
Exposure period: 96 hour(s)
Unit: mg/l Analytical monitoring: no
LC0: .056
LC50: .187
LC100: .56
Method: OECD Guide-line 203 "Fish, Acute Toxicity Test"
Year: GLP: no data
Test substance: as prescribed by 1.1 - 1.4
Remark: Renewal of test medium at 48 hours.
Source: Akzo Nobel Chemicals b.v. Amersfoort
Reliability: (1) Valid without restriction. Guideline study.

(20)

Type: semistatic
Species: Poecilia reticulata (Fish, fresh water)
Exposure period: 96 hour(s)
Unit: mg/l Analytical monitoring: no
LC50: .32
LC100: 1
Method: OECD Guide-line 203 "Fish, Acute Toxicity Test"
Year: GLP: no
Test substance: as prescribed by 1.1 - 1.4
Remark: Renewal of test media at 48 hours.
Source: Akzo Nobel Chemicals b.v. Amersfoort
Reliability: (1) Valid without restriction. Guideline study.

(21)

4.2 Acute Toxicity to Aquatic Invertebrates

Type: static
Species: Daphnia magna (Crustacea)
Exposure period: 48 hours
Unit: mg/l Analytical monitoring: no
Method: EPA-660/3-75-009, Methods for Acute Toxicity Tests with

Fish, Macroinvertebrates and Amphibians
Year: 1975 GLP: Yes
Test substance: As prescribed by 1.1-1.4, purity: 98%%
LC50 (24 hr): 0.31 mg/l
LC50 (48 hr): 0.24 mg/l
NOEC: 0.056 mg/l
Concentrations: 0, 0.032, 0.056, 0.1, 0.18, 0.32 and 0.56 mg/l
Remarks: The acute aquatic toxicity of TETD to Daphnia magna was assessed using the procedures described in Standard Methods for Examination of Water and Wastewater, and Methods for Acute Toxicity Tests with Fish, Macroinvertebrates and Amphibians. There were no deviations from these protocols. An initial range-finding experiment preceded the definitive bioassay. Test vessels, containing 200 ml ABC well water, were kept at 20°C in a temperature controlled area. The lighting was maintained at 50-70 foot-candles on a 16-hour daylight photo-period. Ten Daphnia (first instar less than 24 hours old) per test chamber were selected for each of the six test concentrations and for the controls. Concentrations were tested in duplicate. Nanograde acetone was used as the solvent for the test compound, and for the solvent control. The 24 and 48-hour LC50 values, and their corresponding 95% confidence limits, were determined by an LC50 computer program developed by Stephan et al. using the binomial, moving average angle and probit methods. Water quality parameters of temperature, pH dissolved oxygen were monitored throughout the test and were considered adequate and comparable to those of the controls.
Source: Monsanto ABC-83-048, 1983
Reliability: (1) Valid without restriction

(22)

Type: Static
Species: Daphnia magna (Crustacea)
Exposure period: 48 hour(s)
Unit: mg/l Analytical monitoring: no
EC50: 0.21 mg/l
Method: OECD Guide-line 202, part 1 "Daphnia sp., Acute Immobilisation Test"
Year: 1986 GLP: No data
Test substance: As prescribed by 1.1-1.4, purity: 98%
Remarks: The toxicity of TETD was assessed using the procedures described in OECD 202.
Source: Van Leeuwen, C.J., 1986
Reliability: (4) Unassignable – data from a secondary literature source

(14)

4.3 Toxicity to Aquatic Plants e.g. Algae

Species: Chlorella pyrenoidosa (Algae)
Endpoint: growth rate
Exposure period: 96 hour(s)
Unit: mg/l Analytical monitoring: no
EC50: 1.8 mg/l
Method: OECD Guide-line 201 "Algae, Growth Inhibition Test"
Year: 1986 GLP: no data
Test substance: as prescribed by 1.1 - 1.4, purity: 98%
Source: Van Leeuwen, C.J., 1986
Reliability: (4) Unassignable – data from a secondary literature source

(14)

4.4 Toxicity to Microorganisms e.g. Bacteria

Type: aquatic
Species: Photobacterium phosphoreum (Bacteria)
Exposure period: 15 minutes
Unit: mg/l Analytical monitoring: No data
EC50: 1.21 mg/l
Method: other
Year: 1896 GLP: No data
Test substance: as prescribed by 1.1 - 1.4, purity: 98%
Source: Van Leeuwen, C.J., 1986
Reliability: (4) Unassignable – data from a secondary literature source (14)

Type: aquatic
Species: Nitrosomonas/Nitrobacter (Bacteria)
Exposure period: 3 hours
Unit: mg/l Analytical monitoring: No data
MIC: >320 mg/l
Method: other
Year: 1896 GLP: No data
Test substance: as prescribed by 1.1 - 1.4, purity: 98%
Source: Van Leeuwen, C.J., 1986
Reliability: (4) Unassignable – data from a secondary literature source (14)

5. Toxicity

5.1 Acute Toxicity

5.1.1 Acute Oral Toxicity

Type: LD50
Species: rat
Strain: Sprague-Dawley Albino
Sex: Male and female
Number of Animals: 40 (5/sex/dose)
Vehicle: Corn oil, 382 g/ml
Doses: 2500, 3606, 5200 or 7500 mg/kg bw
Value: 7074 mg/kg bw (combined)
4573 mg/kg bw (females)
>5200 mg/kg bw (estimated for males)
Method: Other: Monsanto EHL Acute Oral Toxicity
Year: 1982 GLP: Yes
Test substance: As prescribed by 1.1-1.4, purity: 98.6%
Remark: Male and female rats (5/sex/dose level) were administered the test substance as a suspension in corn oil via oral intubation. Males ranged in weight from 230-262 grams; females were 166-190 grams. Clinical observations were made three times within the first eight hours after dosing, and twice daily (morning and afternoon) thereafter until sacrifice. Body weights were recorded on days 0, 7 and 14. One 5200 mg/kg male and two 7500 mg/kg males died following traumatic intubations. After 15 days on test, all survivors were humanely sacrificed. Necropsies were performed on all animals. Necropsies included an examination of the animals' exteriors and the contents of the thoracic and abdominal cavities. In one low-dose male rat and two highest-dose female rats, the contents of the cranial cavity were also examined. Clinical signs of toxicity included ataxia, tremors, and an abnormal gait characterized by hopping movements of the hind limbs, lethargy and ptosis. Most surviving animals lost weight during the first week on test. Many of these rats had a notable loss of adipose tissue at necropsy. The acute oral LD50 and 95% confidence limits for female rats and for the combined sexes was calculated using the probit method of Finney (1971). The LD50 value for males was estimated rather than calculated, due to the very low incidence of mortality.

Dose	Morality/Males	Mortality/Females	Combined
2500	1/5	1/5	2/10
3606	0/5	0/5	0/10
5200	0/4	3/5	3/9
7500	0/3	5/5	5/8

Source: Monsanto ML-82-056, EHL Laboratories, 1983
Reliability: (1) Valid without restriction

(23)

Type: LD50
Species: rat
Strain: various
Sex: male/female
Number of Animals: various
Vehicle: various
Value: 500 - 8600 mg/kg bw
Method: various

Year: GLP: no data
Test substance: As prescribed by 1.1-1.4
Remark: Several LD50 studies are reported with results in the range of LD50: 500 to 8600 mg/kg
Source: Akzo Nobel Chemicals b.v. Amersfoort
Reliability: (4) Unassignable – data from secondary literature sources (24)

5.1.2 Acute Inhalation Toxicity

5.1.3 Acute Dermal Toxicity

Type: LD50 (Limit Test)
Species: rabbit
Strain: new Zealand White
Sex: Male and female
Number of Animals: 10
Vehicle: moistened with physiological saline
Doses: 2000 mg/kg bw
Value: >2000 mg/kg bw (combined)
>2000 mg/kg bw (females)
>2000 mg/kg bw (males)
Method: Other: Monsanto EHL Acute Dermal Toxicity, Limit Test
Year: 1982 GLP: Yes
Test substance: As prescribed by 1.1-1.4, purity: 98.6%
Remarks: Young adult rabbits (five males and five females weighing 2.27-2.64 kg) were used for this study. The skin on the dorsal surface of each animal was shaved with electric clippers and abraded with a hypodermic needle prior to test material application. The abrasions were sufficiently deep to penetrate the stratum corneum, but not deep enough to cause bleeding. The test material, moistened with physiological saline, was held in place via an occlusive wrap of latex rubber secured by bandaging and elastic tape. The occlusive wrap was removed 24 hours later, and the excess material wiped from the animal. Clinical observations for signs of toxicity were made three times during the first eight hours on test, and then twice daily (morning and afternoon) until sacrifice. After a 14-day observation period, all animals were sacrificed and necropsied. All animals survived until terminal sacrifice. The only clinical signs of toxicity observed were erythema in the exposed skin of one female and two males, early in the study. At necropsy, one male and two females had off-white fibrous tissue in the hepatic lobes. Two of these animals also had hard, yellow foci in all lobes of the liver, and one had an area of green, necrotic hepatic tissue. All three of these animals also had tapeworm cysts in the mesentery. No abnormalities were noted in the other test animals.

Dose	Mortality/Males	Mortality/Females	Combined
2000	0/5	0/5	0/10

Source: Monsanto ML-82-056, EHL Laboratories, 1983
Reliability: (1) Valid without restriction (25)

Type: LD50
Species: rabbit
Strain:
Sex:
Number of Animals:
Vehicle:

Value: > 2000 mg/kg bw
Method:
Year: 1977 GLP: no
Test substance: as prescribed by 1.1 - 1.4
Source: Akzo Nobel Chemicals b.v. Amersfoort
Reliability: (2) Valid with restrictions – meets generally accepted Scientific method but description lacks detail

(26)

5.2 Corrosiveness and Irritation

5.2.1 Skin Irritation

Species: rabbit
Concentration:
Exposure:
Exposure Time: 4 hours
Number of Animals: 6
PDII: 0
Result: not irritating
EC classificat.: not irritating
Method: other: according to 49 CFR 173.240 (DOT, USA)
Year: 1977 GLP: no
Test substance: as prescribed by 1.1 - 1.4
Remark: Six rabbits were exposed for four hours to the test substance. In 48 hours observation, no effects on the skin were observed.
Source: Akzo Nobel Chemicals b.v. Amersfoort
Reliability: (2) Valid with restrictions – meets generally accepted Scientific method but description lacks detail

(27)

5.2.2 Eye Irritation

Species: rabbit
Concentration: undiluted
Dose: 0.1 g
Exposure Time:
Comment:
Number of Animals: 6
Result: slightly irritating
EC classificat.: not irritating
Method:
Year: 1977 GLP: no
Test substance: as prescribed by 1.1 - 1.4
Remark: 0.1 gram test material was placed in the conjunctival sac of one eye of each of 6 rabbits, the other eye serving as control. In three of the treated animals the eye was washed 20-30 seconds after exposure, in the other animals the eyes remained unwashed.
No effects were observed in the washed eyes. The unwashed eyes showed the material to be slightly irritating only.
Source: Akzo Nobel Chemicals b.v. Amersfoort
Reliability: (2) Valid with restrictions – meets generally accepted Scientific method but description lacks detail

(28)

Species: rabbit
Concentration: undiluted
Dose: 100 mg
Exposure Time:
Comment:
Number of Animals: 6
Result: slightly irritating
EC classificat.: not irritating
Method: other: acc. to AFNOR
Year: 1982 GLP: no data
Test substance: no data
Remark: A 100 mg dose (ground to fine dust) was instilled into the conjunctival sac of one eye, the other eye serving as a control. Scorings were done at t=1 hour and t= 1, 2, 3, 4 and 7 days after instillation. Accroding to the scoring system of AFNOR (Association Francaise de Normalisation) the compouns was a slight eye irritant. All effects had practically disappeared at day 2.
Source: Akzo Nobel Chemicals b.v. Amersfoort
Reliability: (4) Unassignable - data from a secondary literature source (29)

5.3 Sensitization

5.4 Repeated Dose Toxicity

Species: rat Sex: male/female
Strain:
Route of admin.: oral feed
Exposure period: 2 year
Frequency of treatment: daily
Post. obs. period: none
Doses: 100, 300, 1000 and 2500 mg/kg diet
Control Group:
Method:
Year: GLP: no data
Test substance: no data
Remark: Doses given correspond to 5, 15, 50 and 125 mg/kg body weight. Test material was administered via the food. Gross and microscopic effects and effects on growth and mortality were seen at the highest level. Lower dosages showed some effect on growth.
No further details were given.
Source: Akzo Nobel Chemicals b.v. Amersfoort
Reliability: (4) Unassignable - data from a secondary literature source (30)

5.5 Genetic Toxicity 'in Vitro'

Type: Ames Bacterial Reverse Mutation Assay
System of testing: Salmonella typhimurium TA1535, TA1537, TA1538, TA98, TA100
Concentration: 0.1, 1.0, 10.0, 100.0 or 500.0 ug/plate
Cytotoxic Conc.: 500.0 ug/plate
Metabolic activation: with and without
Result: negative with and without activation
Method: EPA/OPPTS 870.5265 and Ames Plate Test (Overlay Method)

Year: 1976 GLP: Yes
Test substance: As prescribed by 1.1-1.4, purity: 98.6%
Remarks: The test compound was evaluated for genetic activity in microbial assays with and without the addition of mammalian metabolic activation preparations. The *Salmonella typhimurium* strains used for this experiment were obtained from Dr. Bruce Ames. The activation system used was S-9 homogenate from Aroclor 1254-induced adult male Sprague-Dawley rat livers. The metabolizing system contained 10% S-9 and cofactors according to the Ames method. The mutagenesis assay was carried out as the plate-incorporation test according to the Ames protocol. Chemicals used as positive controls for the non-activation assays were methylnitrosoguanidine (MNNG), 2-nitrofluorene (NF) and quinacrine mustard (QM). Positive control chemicals used for the activation assays were 2-anthramine (ANTH), 2-acetylaminofluorine (AAF) and 8-aminoquinoline (AMQ). Dimethylsulfoxide (DMSO) was used as the solvent and the solvent control. Analysis included Bartlett's test for homogeneity of variance, and comparison of treatments with controls using within-levels pooled variance and a one-sided t-test. Grubbs' test was performed to determine if outliers were present. The test compound did not demonstrate mutagenic activity in any of the assays conducted and was considered not mutagenic under the test conditions.
Source: Monsanto BIO-77-319, December, 1977
Reliability: (1) Valid without restriction

(31)

Type: Ames Bacterial Reverse Mutation Assay
System of testing: TA1535, TA1537, TA1538, TA98, TA100
Concentration: 10 to 100 ug/plate
Cytotoxic Conc.: no data
Metabolic activation: with and without
Result: negative
Method: Ames Plate Test (Overlay Method)
Year: 1975 GLP: no data
Test substance: no data
Source: Akzo Nobel Chemicals b.v. Amersfoort
Reliability: (4) Unassignable – data from a secondary literature source

(32)

Type: Ames Bacterial Reverse Mutation Assay
System of testing: TA98, TA100, TA1535, TA1537, TA1538
Concentration: 0.5 up to 5000 ug/plate
Cytotoxic Conc.: no data
Metabolic activation: with and without
Result: negative
Method: Ames Plate Test (Overlay Method)
Year: 1975 GLP: no
Test substance: as prescribed by 1.1 - 1.4
Source: Akzo Nobel Chemicals b.v. Amersfoort
Reliability: (2) Valid with restrictions – meets generally accepted Scientific method but description lacks detail

(33)

Type: Ames Bacterial Reverse Mutation Assay
System of testing: TA1535, TA100, TA1538, TA98, TA1537, TA97
Concentration: up to 330 ug/plate
Cytotoxic Conc.: no data
Metabolic activation: with and without
Result: negative
Method: Ames Plate Test (Overlay Method)
Year: 1975 GLP: no
Test substance: as prescribed by 1.1 - 1.4
Source: Akzo Nobel Chemicals b.v. Amersfoort
Reliability: (2) Valid with restrictions – meets generally accepted Scientific method but description lacks detail

(34)

Type: Mitotic Recombination Assay
System of testing: Saccharomyces cerevisiae, D4 (yeast)
Concentration: 0.1, 1.0, 10.0, 100.0 and 500.0 ug/plate
Metabolic activation: With and without
Cytotoxicity conc: With metabolic activation: 500.0 ul/plate
Without metabolic activation: 100.0 ul/plate
Precipitation conc: None
Genotoxic effects: With metabolic activation: Negative
Without metabolic activation: Negative
Method: Ames Mutagenicity Plate Test (Overlay Method) 1975
GLP: Yes
Test substance: As prescribed in 1.1-1.4, purity: 98.6%
Remarks: The test compound was evaluated for genetic activity in assays with and without the addition of mammalian metabolic activation preparations. The activation system used was S-9 homogenate from Aroclor 1254-induced adult male Sprague-Dawley rat livers. The metabolizing system contained 10% S-9 and cofactors according to the Ames method. The mutagenesis assay was carried out as the plate-incorporation test according to the Ames protocol. The chemical used as the positive control for the non-activation assay was methylnitrosoguanidine (MNNG) at 10 ug/plate. Positive control chemical used for the activation assay was DMNA at 100 micromoles/plate. Dimethylsulfoxide (DMSO) was used as the solvent and the solvent control. Analysis included Bartlett's test for homogeneity of variance, and comparison of treatments with controls using within-levels pooled variance and a one-sided t-test. Grubbs' test was performed to determine if outliers were present. The test compound did not demonstrate mutagenic activity in any of the assays conducted and was considered not mutagenic under the test conditions.
Source: Monsanto BIO-77-319, December 1977
Reliability: (1) Valid without restriction

(31)

Type: Mammalian Cell Gene Mutation Assay
System of testing: L5178Y mouse lymphoma cells
Concentration: 0.0006 to 4.1 ug/ml
Cytotoxic Conc.: no data
Metabolic

activation:	without
Result:	positive
Method:	other: no information
Year:	GLP: no data
Test substance:	no data
Remark:	No details on the method used and on the test substance used.
Source:	Akzo Nobel Chemicals b.v. Amersfoort
Reliability:	(4) Unassignable – data from a secondary literature source

(35)

Type:	Sister Chromatid Exchange (SCE)
System of testing:	Chinese Hamster Ovary (CHO) cells (CHO-W-B1)
Concentration:	up to 5 mg/ml
Cytotoxic Conc.:	no data
Metabolic activation:	with and without
Result:	negative
Method:	NTP SCE Protocol
Year:	1979 GLP: yes
Test substance:	As prescribed by 1.1-1.4, purity: 'commercial'
Remark:	TETD was tested in cultured CHO cells for induction of sister chromatid exchanges in the presence and absence of Aroclor 1254-induced male Sprague-Dawley rat liver S9 enzymes and cofactor mix. Cultures were handled under gold lights to prevent photolysis of bromodeoxyuridine-substituted DNA. Concurrent solvent and positive controls were used. At least three doses of the test chemical was used.
Source:	NTP Genetic Toxicology of Tetraethylthiuram Disulfide, 1979
Reliability:	(2) Valid with restrictions. Peer-reviewed published data. Meets generally accepted scientific method but description lacks detail.

(36)

Type:	Mammalian Chromosome Aberration (CA)
System of testing:	Chinese Hamster Ovary (CHO) cells (CHO-W-B1)
Concentration:	up to 5 mg/ml
Cytotoxic Conc.:	no data
Metabolic activation:	with and without
Result:	positive
Method:	NTP SA Protocol
Year:	1979 GLP: yes
Test substance:	As prescribed by 1.1-1.4, purity: 'commercial'
Remark:	TETD was tested in cultured CHO cells for induction of sister chromatid exchanges in the presence and absence of Aroclor 1254-induced male Sprague-Dawley rat liver S9 enzymes and cofactor mix. Cultures were handled under gold lights to prevent photolysis of bromodeoxyuridine-substituted DNA. Concurrent solvent and positive controls were used. At least three doses of the test chemical was used.
Source:	NTP Genetic Toxicology of Tetraethylthiuram Disulfide, 1979
Reliability:	(2) Valid with restrictions. Peer-reviewed published data. Meets generally accepted scientific method but description lacks detail.

(36)

Type: Mammalian Cell Forward Mutation Assay
System of testing: L5178Y Mouse Lymphoma cells
Concentration: up to 5 mg/kg
Cytotoxic Conc.: no data
Metabolic activation: with and without
Result: positive
Method: Clive and Spector, Mutation Research 31: 17-29
Year: 1975 GLP: yes
Test substance: As prescribed by 1.1-1.4, purity: 'commercial'
Remark: The test article was evaluated for specific locus forward mutation in the L5178Y Thymidine Kinase (TK) mouse lymphoma cell assay. The cells used are heterozygous for a specific autosomal mutation at the TK locus and are BUdR sensitive. Scoring for mutation was based on selecting cells that have undergone forward mutation from a TK+/- to a TK-/- genotype by cloning them in soft agar with BUdR. Positive results were reported. All treatment levels, including concurrent positive and solvent controls, were replicated. No other information available.
Source: NTP Genetic Toxicology of Tetraethylthiuram Disulfide, 1979
Reliability: (2) Valid with restrictions. Peer-reviewed published data. Meets generally accepted scientific method but description lacks detail.

(36)

5.6 Genetic Toxicity 'in Vivo'

Type: Cytogenetic assay
Species: rat Sex: female
Strain: Wistar
Route of admin.: other: two groups oral feed and one group oral gavage
Exposure period: 5 days (low and mid dose group), once (high dose group)
Doses: 350, 750 mg/kg/day (feed) and 3300 mg/kg/day (gavage)
Result:
Method: other
Year: GLP: no data
Test substance: no data
Remark: Animals were killed 24 hours after treatment. Minimum of 100 metaphases were scored per animal. Concluded to be non-clastogenic.
Source: Akzo Nobel Chemicals b.v. Amersfoort
Reliability: (4) Unassignable – data from a secondary literature source

(37)

Type: Drosophila SLRL test
Species: Drosophila melanogaster Sex:
Strain:
Route of admin.:
Exposure period:
Doses: 3.7-12.3 mg/ml
Result:
Method:
Year: GLP:
Test substance:
Remark: No details given. Test material was negative, when tested up to 9 days after the treatments.
Source: Akzo Nobel Chemicals b.v. Amersfoort
Reliability: (4) Unassignable – data from a secondary literature source

(38)

Type: Drosophila SLRL test
Species: Drosophila melanogaster Sex:
Strain:
Route of admin.:
Exposure period:
Doses:
Result:
Method:
Year: GLP:
Test substance:
Remark: Result: negative. No further details (eg. concentrations) were given.
Source: Akzo Nobel Chemicals b.v. Amersfoort
Reliability: (4) Unassignable – data from a secondary literature source (38)

Type: Micronucleus assay
Species: mouse Sex: male/female
Strain: Balb/c
Route of admin.: oral unspecified
Exposure period: single dose
Doses: 625, 1250, 2500 mg/kg body weight
Result: negative
Method: other: not specified
Year: 1993 GLP: no data
Test substance: no data
Remark: There was no genotoxic response in the bone marrow of animals of all test groups sampled 24 or 48 hours after dosing.
Source: Akzo Nobel Chemicals b.v. Amersfoort
Reliability: (4) Unassignable – data from a secondary literature source (39)

5.7 Carcinogenicity

Species: rat Sex: male/female
Strain: Fischer 344
Route of admin.: oral feed
Exposure period: 107 weeks
Frequency of treatment: daily
Post. obs. period: None
Doses: 0, 300 or 600 ppm
Result: Negative for both males and females
Control Group: yes, concurrent no treatment
Method: NTP Protocol for 2-Year Carcinogenesis Bioassays
Year: 1979 GLP: Yes
Test substance: As prescribed by 1.1-1.4, purity: >97%
Remark: Groups of 50 rats of each sex were fed the test compound via dietary admixture for 107 weeks. Matched controls consisted of 20 untreated rats of each sex. Individual animal body weights were recorded on Day One on test, and at 4-week intervals thereafter. Animals were observed twice daily, at least 6 hours apart, for moribundity and mortality. Formal examinations for clinical signs of toxicity were made and recorded at 4-week intervals. Complete necropsies were performed on all treated and control animals that either died or were sacrificed. All tissues required for complete histopathologic evaluation of animals that died on test or survived to terminal sacrifice were trimmed, embedded, sectioned and stained with hematoxylin and eosin. Mortality in

the dosed animals was not significantly affected by the test chemical. Mean body weights of the dose rats of both sexes were lower than the corresponding controls, and were dose-related throughout most of the bioassay. No tumors occurred in the rats of either sex at incidences that were significantly higher than in the control group. It was concluded that the test material was not carcinogenic to F344 male and female rats under the conditions of this bioassay.

Source: TR-166, National Toxicology Program, 1979
Reliability: (1) Valid without restriction

(40)

Species: mouse Sex: male/female
Strain: B6C3F1
Route of admin.: oral feed
Exposure period: 108 weeks
Frequency of treatment: daily
Post. obs. period: none
Doses: 0, 100, 500, 2000 ppm
Result: Negative for both males and females
Control Group: yes, concurrent no treatment
Method: NTP Protocol for 2-Year Carcinogenesis Bioassays
Year: 1979 GLP: Yes
Test substance: As prescribed by 1.1-1.4, purity: >97%
Remark: Dose groups consisted of 50 male and 50 female animals. Females were dose 0, 100 or 500 ppm whereas the males were dosed 0, 500 or 2000 ppm. The control group consisted of 20 male and 20 female animals. Individual animal body weights were recorded on Day One on test, and at 4-week intervals thereafter. Animals were observed twice daily, at least 6 hours apart, for moribundity and mortality. Formal examinations for clinical signs of toxicity were made and recorded at 4-week intervals. Complete necropsies were performed on all treated and control animals that either died or were sacrificed. All tissues required for complete histopathologic evaluation of animals that died on test or survived to terminal sacrifice were trimmed, embedded, sectioned and stained with hematoxylin and eosin. All surviving animals were killed at the end of the treatment period. Mean body weights of the dosed mice of both sexes were lower than those of the corresponding controls, and were dose-related throughout most of the bioassay. No tumors occurred at incidences significantly different form the controls. The test material was concluded to be non-carcinogenic in male and female B6C3F1 mice under the conditions of this bioassay.

Source: TR-166, National Toxicology Program, 1979
Reliability: (1) Valid without restriction

(40)

Species: rats Sex: Male/female
Strain: Fisher F344
Route of admin.: dietary
Exposure period: 78 weeks
Frequency of treatment: daily
Post. obs. period: none
Doses: 0.1% TETD

0.2% sodium nitrate
0.1% TETD + 0.2% sodium nitrate

Result: negative for TETD fed alone
Control Group: no data
Method: no data
Year: 1980 GLP: no data
Test substance: As prescribed by 1.1-1.4, purity: 'commercial'
Remark: A study was conducted in which Sodium nitrite and TETD alone and a mixture of 0.1% TETD and 0.2% sodium nitrate were administered to Fisher F344 rats for 78 weeks via their diet. Each group consisted of 20 male and 20 female animals. The rats fed either TETD or sodium nitrite alone did not develop any tumors. Of the animals fed the mixture 10 males and 12 females developed tumors of oesophagus, tongue, squamous stomach or nasal cavity. The author did not attribute the tumors to the separate chemicals but to the reaction of TETD and sodium nitrite in the stomach to nitrosodiethylamine, a nitrosamine which also gave rise to tumors when administered as such.
Source: Lijinsky, W., Food Cosmet Toxicol 18 (1), 1980
Reliability: (4) Unassignable – data from a secondary literature source (41)

5.8 Toxicity to Reproduction

5.9 Developmental Toxicity/Teratogenicity

Species: rat Sex: female
Strain: Sprague-Dawley
Route of admin.: gavage
Exposure period: day 3 to 21 of gestation
Frequency of treatment: once daily
Duration of test:
Doses: 250 mg/kg bodyweight
Control Group: no data specified
NOAEL Maternalt.: > 250 mg/kg bw
NOAEL Teratogen.: > 250 mg/kg bw
Method: other
Year: GLP: no data
Test substance: no data
Remark: The test group only consisted of 4 animals.
The test dose (250 mg/kg bw/day) did not cause maternal toxicity. There were no teratogenic effects seen.
Source: Akzo Nobel Chemicals b.v. Amersfoort
Reliability: (4) Unassignable – data from a secondary literature source (9)

Species: mouse Sex: female
Strain: CD-1
Route of admin.: gavage
Exposure period: days 6-13 of gestation
Frequency of treatment: once per day
Duration of test:
Doses: 4900 mg/kg/day
Control Group: no data specified
NOAEL Maternalt.: > 4900 mg/kg bw
NOAEL Teratogen.: > 4900 mg/kg bw
Method: Other: Proposed new method for short-term in vivo animal Bioassay

Year:	1986 GLP: no data
Test substance:	As prescribed by 1.1-1.4, purity: ‘commercial’
Remark:	50 pregnant mice were dosed with the test material in corn oil by gavage in mid-pregnancy and allowed to go to term. Observations were made on litter size, birth weight, neonatal growth, survival of pups and developmental toxicity. No toxic effects in the treated dams or offspring for the parameters assayed were observed.
Source:	Hardin, BD et al., Teratog Carcinog Mutagen 7, 1987
Reliability:	(4) Unassignable – data from a secondary literature source

(42)

5.10 Other Relevant Information

Type:	other
Remark:	Classified by IARC in Groups 3 'not classifiable as to its carcinogenicity to humans', 1987.
Source:	Akzo Nobel Chemicals b.v. Amersfoort

(9)

5.11 Experience with Human Exposure

Remark:	Alcohol intolerance may occur after exposure to dithiocarbamates. Cases of contact allergy have been reported in literature. Tetraethylthiuram disulfide has been used in the treatment of alcoholism. Articles discussing TETD-, or also called Disulfiram- or Antabuse-, treatment have been published in scientific literature. These studies however are not taken into account for this existing chemicals dossier as they do not reflect occupational situations and because in alcohol therapy therapeutically high doses are used, which do not reflect occupational circumstances. Next to this, in these studies, combination effects of TETD and alcohol cannot be ruled out.
Source:	Akzo Nobel Chemicals b.v. Amersfoort

(9)

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(15) Van Leeuwen, C.J., Ecotoxicological Aspects of Dithiocarbamates, Rijkwaterstaat Communications no. 44, The Netherlands, 1986

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CAS# 137-26-8
Thiram

Molecular Formula: C6H12N2S4
Molecular Weight: 240.4

1. General Information

1.1 General Substance Information

Substance type: organic
Physical status: solid

1.2 Synonyms

a: Thiuram
Source: Chemie GmbH Bitterfeld-Wolfen Wolfen

aa: Fernacol
Source: Chemie GmbH Bitterfeld-Wolfen Wolfen

ab: Fernasan
Source: Chemie GmbH Bitterfeld-Wolfen Wolfen

ac: Fernasan A
Source: Chemie GmbH Bitterfeld-Wolfen Wolfen

ad: Fernide
Source: Chemie GmbH Bitterfeld-Wolfen Wolfen

ae: Flo Pro T Seed Protectant
Source: Chemie GmbH Bitterfeld-Wolfen Wolfen

af: FMC 2070
Source: Chemie GmbH Bitterfeld-Wolfen Wolfen

ag: Formamide, 1,1'-dithiobis(N,N-dimethylthio-
Source: Chemie GmbH Bitterfeld-Wolfen Wolfen

ah: Hermal
Source: Chemie GmbH Bitterfeld-Wolfen Wolfen

ai: Hermat TMT
Source: Chemie GmbH Bitterfeld-Wolfen Wolfen

aj: Heryl
Source: Chemie GmbH Bitterfeld-Wolfen Wolfen

ak: Hexathir
Source: Chemie GmbH Bitterfeld-Wolfen Wolfen

al: Kregasan
Source: Chemie GmbH Bitterfeld-Wolfen Wolfen

am: Mercuram
Source: Chemie GmbH Bitterfeld-Wolfen Wolfen

an: Methyl thiram
Source: Chemie GmbH Bitterfeld-Wolfen Wolfen

ao: Methyl thiuramdisulfide
Source: Chemie GmbH Bitterfeld-Wolfen Wolfen

ap: Methyl tuads
Source: Chemie GmbH Bitterfeld-Wolfen Wolfen

aq: Micropearls
Source: Chemie GmbH Bitterfeld-Wolfen Wolfen

ar: Nobecutan
Source: Chemie GmbH Bitterfeld-Wolfen Wolfen

as: Nomersan
Source: Chemie GmbH Bitterfeld-Wolfen Wolfen

at: Normersan
Source: Chemie GmbH Bitterfeld-Wolfen Wolfen

au: Panoram 75
Source: Chemie GmbH Bitterfeld-Wolfen Wolfen

av: Polyram ultra
Source: Chemie GmbH Bitterfeld-Wolfen Wolfen

aw: Pomarsol
Source: Chemie GmbH Bitterfeld-Wolfen Wolfen

ax: Pomarsol forte
Source: Chemie GmbH Bitterfeld-Wolfen Wolfen

ay: Pomasol
Source: Chemie GmbH Bitterfeld-Wolfen Wolfen

az: Puralin
Source: Chemie GmbH Bitterfeld-Wolfen Wolfen

b: Thioperoxydicarbonicdiamide, tetramethyl-
Source: Chemie GmbH Bitterfeld-Wolfen Wolfen

ba: Radothiram
Source: Chemie GmbH Bitterfeld-Wolfen Wolfen

bb: RCRA waste number U244
Source: Chemie GmbH Bitterfeld-Wolfen Wolfen

bc: Rezifilm
Source: Chemie GmbH Bitterfeld-Wolfen Wolfen

bd: Royal TMDT

Source: Chemie GmbH Bitterfeld-Wolfen Wolfen

be: Sadoplon
Source: Chemie GmbH Bitterfeld-Wolfen Wolfen

bf: Spotrete
Source: Chemie GmbH Bitterfeld-Wolfen Wolfen

bg: Spotrete-F
Source: Chemie GmbH Bitterfeld-Wolfen Wolfen

bh: SQ 1489
Source: Chemie GmbH Bitterfeld-Wolfen Wolfen

bi: Tersan
Source: Chemie GmbH Bitterfeld-Wolfen Wolfen

bis(dimethylthiocarbamoyl)disulfide
Source: UCB-Chemicals Gent

Bis(dimethylthiocarbamoyl)disulfide
Source: Akzo Nobel Chemicals GmbH Dueren

bis(dimethylthiocarbamy)disulfide
Source: UCB-Chemicals Gent

bis(dimethylthiocarbamyl)disulfide; tetramethylthiuram bisulfide; N,N,N',N'-
Source: UCB CHEMICALS BRUSSELS

bj: Tersan 75
Source: Chemie GmbH Bitterfeld-Wolfen Wolfen

bk: Tetramethyldiurane sulphite
Source: Chemie GmbH Bitterfeld-Wolfen Wolfen

bl: Tetramethylenethiuram disulphide
Source: Chemie GmbH Bitterfeld-Wolfen Wolfen

bm: Tetramethylthiocarbamoyldisulphide
Source: Chemie GmbH Bitterfeld-Wolfen Wolfen

bn: Tetramethylthioperoxydicarbonic diamide
Source: Chemie GmbH Bitterfeld-Wolfen Wolfen

bo: Tetramethylthioramdisulfide
Source: Chemie GmbH Bitterfeld-Wolfen Wolfen

bp: Tetramethyl-thiram disulfid
Source: Chemie GmbH Bitterfeld-Wolfen Wolfen

bq: Tetramethylthiuam bisulphide
Source: Chemie GmbH Bitterfeld-Wolfen Wolfen

br: Tetramethylthiuramdisulfid
Source: Chemie GmbH Bitterfeld-Wolfen Wolfen

bs: Tetramethylthiuram disulfide
Source: Chemie GmbH Bitterfeld-Wolfen Wolfen

bt: Tetramethylthiuram disulphide
Source: Chemie GmbH Bitterfeld-Wolfen Wolfen

bu: N,N-Tetramethylthiuram disulphide
Source: Chemie GmbH Bitterfeld-Wolfen Wolfen

bv: N,N,N',N'-Tetramethylthiuram disulfide
Source: Chemie GmbH Bitterfeld-Wolfen Wolfen

bw: Tetramethylthiuran disulphide
Source: Chemie GmbH Bitterfeld-Wolfen Wolfen

bx: Tetramethyl thiurane disulfide
Source: Chemie GmbH Bitterfeld-Wolfen Wolfen

by: Tetramethyl thiurane disulphide
Source: Chemie GmbH Bitterfeld-Wolfen Wolfen

bz: Tetramethylthiurum disulfide
Source: Chemie GmbH Bitterfeld-Wolfen Wolfen

c: Accelerator thiuram
Source: Chemie GmbH Bitterfeld-Wolfen Wolfen

ca: Tetramethylthiurum disulphide
Source: Chemie GmbH Bitterfeld-Wolfen Wolfen

cb: Tetrapom
Source: Chemie GmbH Bitterfeld-Wolfen Wolfen

cc: Tetrathiuram disulfide
Source: Chemie GmbH Bitterfeld-Wolfen Wolfen

cd: Tetrathiuram disulphide
Source: Chemie GmbH Bitterfeld-Wolfen Wolfen

ce: Thillate
Source: Chemie GmbH Bitterfeld-Wolfen Wolfen

cf: Thimer
Source: Chemie GmbH Bitterfeld-Wolfen Wolfen

cg: Thioknock
Source: Chemie GmbH Bitterfeld-Wolfen Wolfen

ch: Thiosan
Source: Chemie GmbH Bitterfeld-Wolfen Wolfen

ci: Thiotox (fungicide)
Source: Chemie GmbH Bitterfeld-Wolfen Wolfen

cj: Thiram
Source: Chemie GmbH Bitterfeld-Wolfen Wolfen

ck: Thiram 75
Source: Chemie GmbH Bitterfeld-Wolfen Wolfen

cl: Thiram 80
Source: Chemie GmbH Bitterfeld-Wolfen Wolfen

cm: Thiram (ACGIH:OSHA)
Source: Chemie GmbH Bitterfeld-Wolfen Wolfen

cn: Thiramad
Source: Chemie GmbH Bitterfeld-Wolfen Wolfen

co: Thiram B
Source: Chemie GmbH Bitterfeld-Wolfen Wolfen

cp: Thirame
Source: Chemie GmbH Bitterfeld-Wolfen Wolfen

cq: Thirasan
Source: Chemie GmbH Bitterfeld-Wolfen Wolfen

cr: Thiulix
Source: Chemie GmbH Bitterfeld-Wolfen Wolfen

cs: Thiurad
Source: Chemie GmbH Bitterfeld-Wolfen Wolfen

ct: Thiuram
Source: Chemie GmbH Bitterfeld-Wolfen Wolfen

cu: Thiuram D
Source: Chemie GmbH Bitterfeld-Wolfen Wolfen

cv: Thiuram disulfide, tetramethyl-
Source: Chemie GmbH Bitterfeld-Wolfen Wolfen

cw: Thiuramin
Source: Chemie GmbH Bitterfeld-Wolfen Wolfen

cx: Thiuram M
Source: Chemie GmbH Bitterfeld-Wolfen Wolfen

cy: Thiuram M rubber accelerator
Source: Chemie GmbH Bitterfeld-Wolfen Wolfen

cz: Thiuram-G
Source: Chemie GmbH Bitterfeld-Wolfen Wolfen

d: Aceto TETD
Source: Chemie GmbH Bitterfeld-Wolfen Wolfen

da: Thiuram-GO
Source: Chemie GmbH Bitterfeld-Wolfen Wolfen

db: Thiuram-P
Source: Chemie GmbH Bitterfeld-Wolfen Wolfen

dc: Thiuram-PO
Source: Chemie GmbH Bitterfeld-Wolfen Wolfen

dd: Thiuramyl
Source: Chemie GmbH Bitterfeld-Wolfen Wolfen

de: Thylate
Source: Chemie GmbH Bitterfeld-Wolfen Wolfen

df: Tigam
Source: Chemie GmbH Bitterfeld-Wolfen Wolfen

dg: Tirampa
Source: Chemie GmbH Bitterfeld-Wolfen Wolfen

dh: Tiuram

Source: Chemie GmbH Bitterfeld-Wolfen Wolfen

di: Tiuramyl
Source: Chemie GmbH Bitterfeld-Wolfen Wolfen

Diamida de tetrametil-tioperoxidicarbónico
Source: GENERAL QUIMICA, S.A. LANTARON COMUNION (ALAVA)

Disulfuro de bis(dimetiltiocarbamilo)
Source: GENERAL QUIMICA, S.A. LANTARON COMUNION (ALAVA)

Disulfuro de tetrametiltiuram
Source: GENERAL QUIMICA, S.A. LANTARON COMUNION (ALAVA)

dj: TMTD
Source: Chemie GmbH Bitterfeld-Wolfen Wolfen

dk: TMTDS
Source: Chemie GmbH Bitterfeld-Wolfen Wolfen

dl: Trametan
Source: Chemie GmbH Bitterfeld-Wolfen Wolfen

dm: Tridipam
Source: Chemie GmbH Bitterfeld-Wolfen Wolfen

dn: Tripomol
Source: Chemie GmbH Bitterfeld-Wolfen Wolfen

do: Tuads
Source: Chemie GmbH Bitterfeld-Wolfen Wolfen

dp: TUEX
Source: Chemie GmbH Bitterfeld-Wolfen Wolfen

dq: Tulisan
Source: Chemie GmbH Bitterfeld-Wolfen Wolfen

dr: USAF B-30
Source: Chemie GmbH Bitterfeld-Wolfen Wolfen

ds: USAF EK-2089
Source: Chemie GmbH Bitterfeld-Wolfen Wolfen

dt: USAF P-5
Source: Chemie GmbH Bitterfeld-Wolfen Wolfen

du: Vancida TM-95
Source: Chemie GmbH Bitterfeld-Wolfen Wolfen

dv: Vancide TM
Source: Chemie GmbH Bitterfeld-Wolfen Wolfen

dw: VUAgT-I-4
Source: Chemie GmbH Bitterfeld-Wolfen Wolfen

dx: Vulcafor TMTD
Source: Chemie GmbH Bitterfeld-Wolfen Wolfen

dy: Vulkacit MTIC
Source: Chemie GmbH Bitterfeld-Wolfen Wolfen

dz: Vulkacit thiuram
Source: Chemie GmbH Bitterfeld-Wolfen Wolfen

e: Arasan
Source: Chemie GmbH Bitterfeld-Wolfen Wolfen

ea: Vulkacit thiuram/C
Source: Chemie GmbH Bitterfeld-Wolfen Wolfen

eb: Wobezit-Thiuram
Source: Chemie GmbH Bitterfeld-Wolfen Wolfen

ec: ZUPA S 80
Source: Chemie GmbH Bitterfeld-Wolfen Wolfen

f: Arasan 70
Source: Chemie GmbH Bitterfeld-Wolfen Wolfen

g: Arasan 75
Source: Chemie GmbH Bitterfeld-Wolfen Wolfen

h: Arasan-M
Source: Chemie GmbH Bitterfeld-Wolfen Wolfen

i: Arasan 42-S
Source: Chemie GmbH Bitterfeld-Wolfen Wolfen

j: Arasan-SF
Source: Chemie GmbH Bitterfeld-Wolfen Wolfen

k: Arasan-SF-X
Source: Chemie GmbH Bitterfeld-Wolfen Wolfen

l: Aules
Source: Chemie GmbH Bitterfeld-Wolfen Wolfen

m: Bis((dimethylamino)carbonothioyl) disulphide
Source: Chemie GmbH Bitterfeld-Wolfen Wolfen

N,N,N',N'-tetramethylthiuram disulfide
Source: UCB-Chemicals Gent

n: Bis(dimethyl-thiocarbamoyl)-disulfid
Source: Chemie GmbH Bitterfeld-Wolfen Wolfen

Nombre comercial: Rubator DTMT
Source: GENERAL QUIMICA, S.A. LANTARON COMUNION (ALAVA)

o: Bis(dimethylthiocarbamoyl) disulfide
Source: Chemie GmbH Bitterfeld-Wolfen Wolfen

p: Bis(dimethylthiocarbamoyl) disulphide
Source: Chemie GmbH Bitterfeld-Wolfen Wolfen

q: Bis(dimethylthiocarbamyl) disulfide
Source: Chemie GmbH Bitterfeld-Wolfen Wolfen

r: Chipco thiram 75
Source: Chemie GmbH Bitterfeld-Wolfen Wolfen

s: Cyuram DS
Source: Chemie GmbH Bitterfeld-Wolfen Wolfen

t: Disolfuro di tetrametiltiourame
Source: Chemie GmbH Bitterfeld-Wolfen Wolfen

Tetra Methyl Thiuram Disulphide
Source: NORKEM LIMITED KNUTSFORD

tetramethylthiuram bisulfide
Source: UCB-Chemicals Gent

Tetramethylthiuram disulfide; Thioperoxidicarbonic diamide, tetramethyl; Bis(dimethylthiocarbamoyl)disulfide; TMTD
Source: M.L.P.C. RION DES LANDES

tetramethylthiuram disulfide;thiuram disulfide, tetramethyl-, thiuram TMTD
Source: UCB CHEMICALS BRUSSELS

Tetramethylthiuram disulphide
Source: UCB-Chemicals Gent

Tetramethylthiuram disulphide; bis(dimethylthiocarbamoyl)disulfide;
Source: UCB CHEMICALS BRUSSELS

Thioperoxydicarbonic diamide, tetramethyl (CAS-name)
Source: Akzo Nobel Chemicals GmbH Dueren

Thiram
Source: UCB-Chemicals Gent
Akzo Nobel Chemicals GmbH Dueren

thiuram disulfide, tetramethyl-, thiuram TMTD thiuramyl
Source: UCB-Chemicals Gent

thiuramyl; TMT; TMTD; TMTDS; Thiram.
Source: UCB CHEMICALS BRUSSELS

TMT
Source: UCB-Chemicals Gent

TMTD
Source: UCB-Chemicals Gent
GENERAL QUIMICA, S.A. LANTARON COMUNION (ALAVA)
ISAGRO SPA SEGRATE (MI)
Akzo Nobel Chemicals GmbH Dueren
TMTDS
Source: UCB-Chemicals Gent

u: Disulfure de tetramethylthiourame
Source: Chemie GmbH Bitterfeld-Wolfen Wolfen

v: alpha,alpha'-Dithiobis(dimethylthio)formamide
Source: Chemie GmbH Bitterfeld-Wolfen Wolfen

w: N,N'-(Dithiodicarbonothioyl)bis(N-methylmethanamine)
Source: Chemie GmbH Bitterfeld-Wolfen Wolfen

x: Ekagom TB
Source: Chemie GmbH Bitterfeld-Wolfen Wolfen

y: Falitiram
Source: Chemie GmbH Bitterfeld-Wolfen Wolfen

z: Fermide
Source: Chemie GmbH Bitterfeld-Wolfen Wolfen

1.3 Impurities

1.4 Additives

2. Physico-chemical Data

2.1 Melting Point

Value: ca. 145 degree C
Decomposition: yes
Method: OECD Guide-line 102 "Melting Point/Melting Range"
Year: 1981
GLP: no
Source: UCB CHEMICALS BRUSSELS
UCB-Chemicals Gent
Reliability: (1) Valid without restriction
(1)

Value: 146 degree C
GLP: no
Source: Akzo Nobel Chemicals GmbH Dueren
Reliability: (1) Valid without restriction

Value: 155.6 degree C
Method: other
GLP: no data
Source: Akzo Nobel Chemicals GmbH Dueren
Reliability: (1) Valid without restriction
(2)

2.2 Boiling Point

Value: 129 degree C at 26.7 hPa
Decomposition: yes
Method: other
GLP: no data
Remark: 129 degrees C at 20mm Hg.
Source: GENERAL QUIMICA, S.A. LANTARON COMUNION (ALAVA)
Reliability: (1) Valid without restriction
(3)

Value: 129 degree C at 27 hPa
Year: 1988
GLP: no data
Source: Akzo Nobel Chemicals GmbH Dueren
Reliability: (1) Valid without restriction
(4)

2.3 Density

Type: density
Value: = 1.29 g/cm3 at 20 degree C
Method: other
GLP: no data
Source: GENERAL QUIMICA, S.A. LANTARON COMUNION (ALAVA)
Reliability: (1) Valid without restriction

Type: bulk density
Value: 460 - 500 kg/m3 at 20 degree C
Source: Akzo Nobel Chemicals GmbH Dueren
Reliability: (1) Valid without restriction

Type: density
Value: = 1425 kg/m3 at 20 degree C
Source: Akzo Nobel Chemicals GmbH Dueren
Reliability: (1) Valid without restriction

Type: bulk density
Value: ca. .32 g/cm3 at 20 degree C
GLP: no
Remark: method : CIPAC nt 39
Source: UCB CHEMICALS BRUSSELS
Reliability: (1) Valid without restriction

(5)

2.4 Vapour Pressure

Value: < .00001 hPa at 25 degree C
Year: 1983
GLP: no data
Source: Akzo Nobel Chemicals GmbH Dueren
Reliability: (1) Valid without restriction

Value: = .000023 hPa at 25 degree C
Method: OECD Guide-line 104 "Vapour Pressure Curve"
Year: 1981
GLP: no
Source: UCB CHEMICALS BRUSSELS
UCB-Chemicals Gent
Reliability: (1) Valid without restriction

(6)

2.5 Partition Coefficient

log Pow: = 1.73 at 20 degree C
Method: OECD Guide-line 107 "Partition Coefficient (n-octanol/water), Flask-shaking Method"
Year: 1981
GLP: no
Source: UCB CHEMICALS BRUSSELS
UCB-Chemicals Gent
Reliability: (1) Valid without restriction

(7)

2.6.1 Water Solubility

Value: ca. 16.5 mg/l at 20 degree C
Qualitative: slightly soluble (0.1-100 mg/L)
pKa: -6 at 25 degree C
pH: ca. 7 at 40 g/l and 20 degree C
Year: 1974
GLP: no
Remark: method : ASTM E70-74
Source: UCB-Chemicals Gent
Reliability: (1) Valid without restriction

(8)

Value: 30 mg/l at 20 degree C
Qualitative: of low solubility
Method: other
Year: 1987
GLP: no data
Source: Akzo Nobel Chemicals GmbH Dueren
Reliability: (1) Valid without restriction

(9)

2.6.2 Surface Tension

2.7 Flash Point

Value: ca. 150 degree C
Type: other
Method: ASTM D 92-96 Test Method for Flash and Fire Points by Cleveland Open Cup
Year: 1992 (Revised 1996)
Remark: Method: Cleveland Open Cup
Source: Akzo Nobel Chemicals GmbH Dueren
Reliability: (1) Valid without restriction

2.8 Auto Flammability

Value:
Remark: not self-flammable
Source: UCB CHEMICALS BRUSSELS
Reliability: (1) Valid without restriction

2.10 Explosive Properties

Result:
Remark: Not explosive
Source: UCB CHEMICALS BRUSSELS
Reliability: (1) Valid without restriction

2.11 Oxidizing Properties

Result:
Remark: not an oxidizer (is not reacting with cellulose or saw dust)
Source: UCB CHEMICALS BRUSSELS
Reliability: (1) Valid without restriction

3. Environmental Fate and Pathways

3.1.1 Photodegradation

Type: air
Light source: Sun light
Spectr.of subst.: lambda (max, >295nm): 242 nm
epsilon (max): 4.1
Conc. of subst.: at 25 degree C
INDIRECT PHOTOLYSIS
Sensitizer: OH

Conc. of sens.: 800000 molecule/cm3
Degradation: = 50 % after 26.6 day
Method: other (calculated)
Year: 1986 GLP: no data
Test substance: as prescribed by 1.1 - 1.4
Source: GENERAL QUIMICA, S.A. LANTARON COMUNION (ALAVA)
Reliability: (2) Valid with restrictions – modeling data

Type: soil
Light source: Xenon lamp
Light spect.: 300 - 750 nm
Rel. intensity: 2 based on Intensity of Sunlight
Conc. of subst.: .317 mg/l
DIRECT PHOTOLYSIS
Halflife t1/2: 17.2 day
Method:
Year: 1987 GLP: yes
Test substance: other TS
Source: Akzo Nobel Chemicals GmbH Dueren
Test substance: 97.7% C14-Thiram was used.
Reliability: (1) Valid without restriction

(10) (11)

Type: water
Light source: Xenon lamp
Light spect.: 290 nm
Rel. intensity: >=
Spectr.of subst.: lambda (max, >295nm): .4 nm
epsilon (max): 7279
Conc. of subst.: 10 mg/l
DIRECT PHOTOLYSIS
Halflife t1/2: ca. 4.1 hour(s)
Degradation: ca. 2 % after 24 hour(s)
Quantum yield: 2.97
Method:
Year: 1990 GLP: yes
Test substance: other TS: 14 C-Thiram
Remark: Method : "Richtlinien f□r die Pr□fung von Pflanzenschutzmitteln im Zulassungsverfahren Teil IV,6-1; Biologische Bundesanstalt (BBA), D-38104 Braunschweig (1990)
Testing at ph7 (buffered system)
Source: UCB CHEMICALS BRUSSELS
Reliability: (1) Valid without restriction

(12)

3.1.2 Stability in Water

Type: abiotic
t1/2 pH7: 2 day at 25 degree C
t1/2 pH9: 4 - 7 hour(s) at 25 degree C
t1/2 pH5: 77 day at 25 degree C
Method: other
Year: 1987 GLP: yes
Test substance: other TS
Source: Akzo Nobel Chemicals GmbH Dueren
Test substance: 97.4% test substance was used
Reliability: (1) Valid without restriction

(13)

Type: biotic
t1/2 pH 7.8 : 46 hour(s) at 20 degree C
Degradation: 90 % after 153 hour(s)
Method: other: BBA Teil IV : 5-1 (1990)
Year: 1990 GLP: yes
Test substance: other TS: 14c- Thiram, 99.7 % radiochemical purity
Source: UCB CHEMICALS BRUSSELS
Test substance: conc. of substance : 1.1 mg/l (nominal)

Degradation products (water phase) - carbon disulphide (CAS75-15-0):
max 0.073 % at day 4; nil at day 14.

dimethyldithiocarbamic acid, methyl ester :
0.076 % max at day 4, nil at day 57.

Reliability: (1) Valid without restriction

(14)

3.1.3 Stability in Soil

Type: laboratory Radiolabel: yes
Concentration: 20.367 mg/kg
Soil humidity: 14.4 g water/100g soil dry weight
Soil classif.: USDA Year:
Content of clay: 14.8 %
silt: 29.6 %
sand: 55.6 %
Organ. carbon: 2.4 %
pH: 6.7
Cation exch.
capac. 14.4 meq/100 g soil dry weight
Microbial
biomass: 39.1 mg biomass/100 g soil dry weight
Dissipation time
DT50: ca. .5 day
DT90: ca. 6 day
Dissipation: 100 % after 128 day
Method: other: EPA/FIFRA u 162-1
Year: 1982 GLP: yes
Test substance: other TS: C-Thiram 98.4 % radiochemical purity
Source: UCB CHEMICALS BRUSSELS
Type: laboratory Radiolabel: no
Concentration: 76 mg/kg
Soil temp.: 22 degree C
Content of clay: 38 %
silt: 10 %
sand: 52 %
Organ. carbon: .5 %
pH: 5
Cation exch.
capac. 3 meq/100 g soil dry weight
Microbial
biomass:
Method: other
Year: 1988 GLP: yes
Test substance: other TS
Remark: Halflife 42.7 days. The test substance has a short half-life and no apparent leaching potential.
Source: Akzo Nobel Chemicals GmbH Dueren
Test substance: 77.3% A.I. material was used
Reliability: (1) Valid without restriction

(15)

3.3.1 Transport between Environmental Compartments

Type: other
Media: water - soil
Air (Level I):
Water (Level I):
Soil (Level I):
Biota (L.II/III):
Soil (L.II/III):
Method: other
Year: 1986
Remark: Concentrations used: 0.1, 0.5, 1.0 and 10 ppm

Soil type	Adsorp. Coeff.	Desorp.
Sand	3.74	75.9
Sandy loam	13.6	5.4
Clay loam	36.6	235
Florida muck	78.3	196

Soil type	Adsorp. Constant	Desorp.
Sand	4300	87240
Sandy loam	951	3590
Clay loam	1620	10400
Florida muck	261	653

The chemical has slight mobility trough sand and low mobility through sandy loam, clay loam and Florida muck. Percent desorbed is low in all test systems; material is readily incorporated in soil matrix.
Source: Akzo Nobel Chemicals GmbH Dueren
Test substance: 98.9% A.I. C14-Thiram was used
Reliability: (1) Valid without restriction

(16)

3.3.2 Distribution

3.5 Biodegradation

Type: aerobic
Inoculum: predominantly domestic sewage, non-adapted
Concentration: 2 mg/l related to Test substance
Degradation: = 100 % after 28 day
Result: readily biodegradable
Method: OECD Guide-line 301 D "Ready Biodegradability: Closed Bottle Test"
Year: 1992 GLP:
Test substance: as prescribed by 1.1 - 1.4
Remark: Because of the high oxygen consumption the percentage biodegradation was calculated for three different ThOD-values with breakdown of N to NH3 or HNO3, and S to H2S or H2SO4.

The results form the biodegradation test are then as follows:
ThOD (NH3, H2S) : 174 % degradation in 28 days

ThOD (HNO3, H2S) : 101 % degradation in 28 days
ThOD (HNO3, H2SO4): 54 % degradation in 28 days

After 28 days, the Closed Bottle Test was continued for two additional weeks (day 42) and no further increase in degradation was found.
Therefore it is concluded that the substance is completely mineralized in 28 days.

Source: Akzo Nobel Chemicals GmbH Dueren
Reliability: (1) Valid without restriction

(17)

Type: aerobic
Inoculum: predominantly domestic sewage, non-adapted
Concentration: 100 mg/l related to Test substance
Degradation: 0 % after 28 day
Result: under test conditions no biodegradation observed
Method: other: MITI test nach Dr. Painter
Year: GLP: no data
Test substance: as prescribed by 1.1 - 1.4
Remark: A relatively high concentration of test substance was used, which may have caused initial toxicity to the test system.
Source: Akzo Nobel Chemicals GmbH Dueren
Reliability: (1) Valid without restriction

(18)

3.6 BOD5, COD or BOD5/COD Ratio

3.7 Bioaccumulation

Species:
Exposure period: at 25 degree C
Concentration:
BCF: 91
Elimination: no
Method: other: not specified
Year: 1983 GLP: no data
Test substance: no data
Remark: The results suggest that Thiram will not bioconcentrate in aquatic species
Source: GENERAL QUIMICA, S.A. LANTARON COMUNION (ALAVA)
Reliability: (1) Valid without restriction

(19)

4. Ecotoxicity

AQUATIC ORGANISMS

4.1 Acute/Prolonged Toxicity to Fish

Type: static
Species: Pimephales promelas(Fish, fresh water)
Exposure period: 96 hours
Unit: mg/l Analytical monitoring: no
Method: EPA-660/3-75-009, Methods for Acute Toxicity Tests with Fish, Macroinvertebrates and Amphibians
Year: 1975 GLP: Yes
Test substance: As prescribed by 1.1-1.4, purity >97%
LC50 (24 hr): 0.38 mg/l

LC50 (48 hr): 0.27 mg/l
LC50 (96 hr): 0.27 mg/l
LOEC: 0.18 mg/l
NOEC: 0.10 mg/l
Concentrations: 0, 0.1, 0.18, 0.32, 0.56 and 1.0 mg/l
Remark: The acute toxicity of TMTD to fathead minnows was assessed using the methods outlined by the USEPA Committee on Methods for Toxicity Tests with Aquatic Organisms. There were no deviations from this protocol. Water quality parameters of temperature, dissolved oxygen and pH were measured throughout the test and remained within acceptable limits. As a quality check, the test fish were challenged with the reference compound Antimycin A, indicating that the fish were in good condition. Ten fish, mean standard weight 0.10 grams and mean standard length 18 mm, were used in each test concentration and controls. A 96-hour range-finding study preceded the definitive test. Nanograde acetone was used as the test compound solvent and as the solvent control. Test fish were placed in the test aquaria within 20 minutes after addition of the test compound aliquots. All concentrations were observed once every 24 hours for mortality and abnormal effects. Statistical analysis of the concentration/effect data was obtained using a computerized LC50 program developed by Stephan et al. This program calculated the LC50 statistic and 95% confidence limits using the binomial, the moving average and the probit tests.
Source: Monsanto AB-84-008, 1983
Reliability: (1) Valid without restriction

(20)

Type: static
Species: Lepomis macrochirus(Fish, fresh water)
Exposure period: 96 hours
Unit: mg/l Analytical monitoring: no
Method: EPA-660/3-75-009, Methods for Acute Toxicity Tests with Fish, Macroinvertebrates and Amphibians
Year: 1975 GLP: Yes
Test substance: As prescribed by 1.1-1.4, purity >97%
LC50 (24 hr): 0.18 mg/l
LC50 (48 hr): 0.14 mg/l
LC50 (96 hr): 0.13 mg/l
LOEC: 0.056 mg/l
NOEC: <0.056 mg/l
Concentrations: 0, 0.056, 0.1, 0.18, 0.32 and 0.56 mg/l
Remark: The acute toxicity of TMTD to bluegill sunfish was assessed using the methods outlined by the USEPA Committee on Methods for Toxicity Tests with Aquatic Organisms. There were no deviations from this protocol. Water quality parameters of temperature, dissolved oxygen and pH were measured throughout the test and remained within acceptable limits. As a quality check, the test fish were challenged with the reference compound Antimycin A, indicating that the fish were in good condition. Ten fish, mean standard weight 0.09 grams and mean standard length 16 mm, were used in each test concentration and controls. A 96-hour range-finding study preceded the definitive test. Nanograde acetone was used as the test compound solvent and as the solvent control. Test fish were placed in the test aquaria within 20 minutes after addition of the test compound aliquots. All concentrations were observed once every 24 hours for mortality and abnormal effects. Statistical analysis of the concentration/effect data was obtained using a computerized LC50 program developed by

Stephan et al. This program calculated the LC50 statistic and 95% confidence limits using the binomial, the moving average and the probit tests.
Source: Monsanto AB-83-058, 1983
Reliability: (1) Valid without restriction

(21)

Type: static
Species: Salmo gairdneri(Fish, fresh water)
Exposure period: 96 hours
Unit: mg/l Analytical monitoring: no
Method: EPA-660/3-75-009, Methods for Acute Toxicity Tests with Fish, Macroinvertebrates and Amphibians
Year: 1975 GLP: Yes
Test substance: As prescribed by 1.1-1.4, purity >97%
LC50 (24 hr): 0.32 mg/l
LC50 (48 hr): 0.16 mg/l
LC50 (96 hr): 0.13 mg/l
LOEC: 0.10 mg/l
NOEC: 0.032 mg/l
Concentrations: 0, 0.032, 0.056, 0.10, 0.18 and 0.32 mg/l
Remark: The acute toxicity of TMTD to rainbow trout was assessed using the methods outlined by the USEPA Committee on Methods for Toxicity Tests with Aquatic Organisms. There were no deviations from this protocol. Water quality parameters of temperature, dissolved oxygen and pH were measured throughout the test and remained within acceptable limits. As a quality check, the test fish were challenged with the reference compound Antimycin A, indicating that the fish were in good condition. Ten fish, mean standard weight 0.89 grams and mean standard length 40 mm, were used in each test concentration and controls. A 96-hour range-finding study preceded the definitive test. Nanograde acetone was used as the test compound solvent and as the solvent control. Test fish were placed in the test aquaria within 20 minutes after addition of the test compound aliquots. All concentrations were observed once every 24 hours for mortality and abnormal effects. Statistical analysis of the concentration/effect data was obtained using a computerized LC50 program developed by Stephan et al. This program calculated the LC50 statistic and 95% confidence limits using the binomial, the moving average and the probit tests.
Source: Monsanto AB-83-047, 1983
Reliability: (1) Valid without restriction

(22)

Type: semistatic
Species: Brachydanio rerio (Fish, fresh water)
Exposure period: 9 day
Unit: µg/l Analytical monitoring: no
Method: OECD Guide-line 204 "Fish, Prolonged Toxicity Test: 14-day Study"
Year: 1984 GLP: no
Test substance: other TS
Remark: Renewal of test media after 48 hours.
Results: NOEC survival : 1 uG/L
NOEC hatching : 0.32 uG/L
NOEC malformations : 3.2 uG/L
Source: Akzo Nobel Chemicals GmbH Dueren
Test substance: 97.9 % A.I. Test material
Reliability: (1) Valid without restriction - Guideline study

(23)

Type: semistatic
Species: Poecilia reticulata (Fish, fresh water)
Exposure period: 96 hour(s)
Unit: mg/l Analytical monitoring: no data
LC50: .27
Method: OECD Guide-line 203 "Fish, Acute Toxicity Test"
Year: 1986 GLP: no
Test substance: other TS
Remark: Test media were renewed every 24 hours.
Source: Akzo Nobel Chemicals GmbH Dueren
Test substance: Purity >= 98 %
Reliability: (1) Valid without restriction - Giudeline study

(24)

Type: semistatic
Species: Poecilia reticulata (Fish, fresh water)
Exposure period: 96 hour(s)
Unit: µg/l Analytical monitoring: no
LC50: 6
LC100: 10
Method: OECD Guide-line 203 "Fish, Acute Toxicity Test"
Year: 1984 GLP: no
Test substance: other TS
Remark: Renewal of test media after 48 hours
Source: Akzo Nobel Chemicals GmbH Dueren
Test substance: 97.9 % A.I. test material was used
Reliability: (1) Valid without restriction - Guideline study

(25)

Type: semistatic
Species: Poecilia reticulata (Fish, fresh water)
Exposure period: 96 hour(s)
Unit: µg/l Analytical monitoring: no
LC0: 3.2
LC50: 8.85
LC100: 32
Method: OECD Guide-line 203 "Fish, Acute Toxicity Test"
Year: 1984 GLP: no
Test substance: other TS
Remark: Renewal of test media after 48 hours
Source: Akzo Nobel Chemicals GmbH Dueren
Test substance: 97.9 % A.I. test material was used
Reliability: (1) Valid without restriction - Guideline study

(26)

Type: semistatic
Species: Poecilia reticulata (Fish, fresh water)
Exposure period: 96
Unit: µg/l Analytical monitoring: no
LC0: 5.6
LC50: 11.1
LC100: 18
Method: OECD Guide-line 203 "Fish, Acute Toxicity Test"
Year: 1987 GLP: no
Test substance: other TS
Remark: Renewal of media after 48 hours
Source: Akzo Nobel Chemicals GmbH Dueren
Test substance: 97.9 % A.I. test material
Reliability: (1) Valid without restriction - Guideline study

(27)

Type: semistatic
Species: Salmo gairdneri (Fish, estuary, fresh water)
Exposure period: 60 day
Unit: µg/l Analytical monitoring: no
LC50: 1.1
EC50 : .65
Method: other
Year: 1986 GLP: no
Test substance: other TS
Remark: A further series of studies were conducted which describes the aquatic toxicity and embryolarval of dithiocarbamates in rainbow trout.
References:
van Leeuwen, C.J. (1986) Dithiocarbamates, a hazard to aquatic ecosystem functioning. Environ, Contam., Int. Conf., 2nd: 215-217.
van Leeuwen, C.J. et al. (1986). Aquatic toxicological aspects of dithiocarbamates and related compounds:III. Embryolarval studies with rainbow trout (Salmo gairdneri). Aquat. Toxicol. (AMST), 9, 129-146.
van Leeuwen, C.J. et al. (1986). Aquatic toxicological aspects of dithiocarbamates and related compounds: IV. teratogenicity and histopathology in rainbow trout (Salmo gairdneri) Aquat. Toxicol. (AMST), 9, 147-160.
van Leeuwen, C.J. et al. (1986). Sublethal effects of tetramethylthiuramdisulfide (Thiram) in rainbow trout (Salmo gairdneri). Aquat. Toxicol. (AMST), 9, 13-20.
Source: Akzo Nobel Chemicals GmbH Dueren
Test substance: 98 % A.I. material
Reliability: (4) Unassignable – data from a secondary literature source

(28)

Type: static
Species: Leuciscus idus (Fish, fresh water)
Exposure period: 96 hour(s)
Unit: mg/l Analytical monitoring: no
LC50: 1.2
Method:
Year: GLP:
Test substance: as prescribed by 1.1 - 1.4
Source: Akzo Nobel Chemicals GmbH Dueren
Reliability: (2) Valid with restrictions – meets generally accepted Scientific method but description lacks detail

(29)

Type: static
Species: Leuciscus idus melanotus (Fish, fresh water)
Exposure period: 96 hour(s)
Unit: mg/l Analytical monitoring: yes
LC0: ca. 0.77
LC50: ca. 1.2
Method: other: not stated
Year: GLP: no
Test substance: other TS: Thiram technical (96.7 % purity)
Source: UCB CHEMICALS BRUSSELS
Reliability: (2) Valid with restrictions – meets generally accepted Scientific method but description lacks detail

(30)

Type: static
Species: Salmo gairdneri (Fish, estuary, fresh water)
Exposure period: 96 hour(s)
Unit: mg/l Analytical monitoring: no
LC50: ca. 0.16
Method:
Year: GLP: no
Test substance:
Remark: method : not stated
Source: UCB CHEMICALS BRUSSELS
Test substance: Thiram technical (96.7 % purity)
Reliability: (2) Valid with restrictions – meets generally accepted Scientific method but description lacks detail

(31)

4.2 Acute Toxicity to Aquatic Invertebrates

Type: static
Species: Daphnia magna (Crustacea)
Exposure period: 48 hours
Unit: mg/l Analytical monitoring: no
Method: EPA-660/3-75-009, Methods for Acute Toxicity Tests with Fish, Macroinvertebrates and Amphibians
Year: 1975 GLP: Yes
Test substance: As prescribed by 1.1-1.4, purity >97%
LC50 (24 hr): 0.31 mg/l
LC50 (48 hr): 0.24 mg/l
NOEC: 0.056 mg/l
Concentrations: 0, 0.032, 0.056, 0.1, 0.18, 0.32 and 0.56 mg/l
Remarks: The acute aquatic toxicity of TMTD to Daphnia magna was assessed using the procedures described in Standard Methods for Examination of Water and Wastewater, and Methods for Acute Toxicity Tests with Fish, Macroinvertebrates and Amphibians. There were no deviations from these protocols. An initial range-finding experiment preceded the definitive bioassay. Test vessels, containing 200 ml ABC well water, were kept at 20°C in a temperature controlled area. The lighting was maintained at 50-70 foot-candles on a 16-hour daylight photo-period. Ten Daphnia (first instar less than 24 hours old) per test chamber were selected for each of the six test concentrations and for the controls. Concentrations were tested in duplicate. Nanograde acetone was used as the solvent for the test compound, and for the solvent control. The 24 and 48-hour LC50 values, and their corresponding 95% confidence limits, were determined by an LC50 computer program developed by Stephan et al. using the binomial, moving average angle and probit methods. Water quality parameters of temperature, pH dissolved oxygen were monitored throughout the test and were considered adequate and comparable to those of the controls.
Source: Monsanto AB-83-048, 1983
Reliability: (1) Valid without restriction

(32)

Type:
Species: Daphnia magna (Crustacea)
Exposure period: 48 hour(s)
Unit: mg/l Analytical monitoring: no
EC50: .21
Method: OECD Guide-line 202, part 1 "Daphnia sp., Acute Immobilisation Test"
Year: 1986 GLP: no

Test substance: other TS
Source: Akzo Nobel Chemicals GmbH Dueren
Test substance: 98 % A.I. test material
Reliability: (1) Valid without restriction - Guideline study

(28)

Type:
Species: Gammarus pulex (Crustacea)
Exposure period:
Unit: Analytical monitoring:
Method:
Year: GLP:
Test substance:
Remark: LC50 calculated for two commercial products (thiram 80%) were in the range of:
- 14 mg/l (24 h) to 0.195 mg/l (96 h) for product A
- 4.77 mg/l (24 h) to 0.13 mg/l (96 h) for product B, in aqueous suspensions
Product A: 80% Thiram, Pomarsol (Bayer)
Product B: 80% Thiram, KB cloque du pecher (Rhodic).
Source: Akzo Nobel Chemicals GmbH Dueren
Reliability: (2) Valid with restrictions - calculation/modeling data

(33)

4.3 Toxicity to Aquatic Plants e.g. Algae

Species: Chlorella pyrenoidosa (Algae)
Endpoint: growth rate
Exposure period: 96 hour(s)
Unit: mg/l Analytical monitoring: no
EC50: 1
Method: OECD Guide-line 201 "Algae, Growth Inhibition Test"
Year: GLP: no data
Test substance: as prescribed by 1.1 - 1.4
Source: Akzo Nobel Chemicals GmbH Dueren
Reliability: (1) Valid without restriction - Guideline study

(28)

Species: Scenedesmus acutus (Algae)
Endpoint: growth rate
Exposure period: 72 hours
Unit: mg/l Analytical monitoring:
Method:
Year: GLP:
Test substance:
Remark: After 5 days there is a decrease of 57.2% in growth at 0.5 mg/l thiram.
After 72 hour Thiram was lethal to the algae at 10 mg/l. The decrease of growth was 16.9% for 500 ppb Thiram.
Source: Akzo Nobel Chemicals GmbH Dueren
Test condition: The growth rate of the algae was monitored by optical density (OD) measurements, microscopic examination and visible observations regarding the color of the culture and sedimentation effect.
The test was conducted at 28 deg. C.
Ethyl alcohol was used as co-solvent.
Reliability: (2) Valid with restrictions - meets generally accepted Scientific method but description lacks detail

(34)

Species: Selenastrum capricornutum (Algae)
Endpoint: growth rate
Exposure period: 120 hour(s)
Unit: mg/l Analytical monitoring: yes
NOEC: ca. 0.0057
EC50: .076
Method:
Year: 1982 GLP: yes
Test substance:
Remark: Method : EPA/FIFRA u 122-2/123-2
Source: UCB CHEMICALS BRUSSELS
Test substance: Thiram technical (99 % purity)
Reliability: (2) Valid with restrictions - meets generally accepted Scientific method but description lacks detail

(35)

4.4 Toxicity to Microorganisms e.g. Bacteria

Type: aquatic
Species: Pseudomonas putida (Bacteria)
Exposure period:
Unit: mg/l Analytical monitoring: yes
EC0: > 200
EC10: > 200
Method: other
Year: 1991 GLP: no
Test substance: as prescribed by 1.1 - 1.4
Source: Akzo Nobel Chemicals GmbH Dueren
Test condition: Robra-test. EC50 is the concentration at which a 50% reduction in oxygen consumption is measured.
The highest practical concentration was used. Due to the low solubility a higher concentration was not possible.
Reliability: (2) Valid with restrictions - meets generally accepted Scientific method but description lacks detail

(36)

4.5 Chronic Toxicity to Aquatic Organisms

4.5.1 Chronic Toxicity to Fish

Species: Salmo gairdneri (Fish, estuary, fresh water)
Endpoint: other
Exposure period: 21 day
Unit: mg/l Analytical monitoring: no
NOEC: .0032
LC50 : < .0081
Method: OECD Guide-line 204
Year: 1984 GLP: yes
Test substance:
Source: UCB CHEMICALS BRUSSELS
Test substance: Thiram technical (99.7 % purity)
Reliability: (1) Valid without restriction - Guideline study

(37)

4.5.2 Chronic Toxicity to Aquatic Invertebrates

Species: Daphnia magna (Crustacea)
Endpoint: mortality
Exposure period: 21 day
Unit: µg/l Analytical monitoring: no

EC50: 8
Method: other
Year: 1986 GLP: no
Test substance: other TS
Source: Akzo Nobel Chemicals GmbH Dueren
Test substance: 98 % A.I. test material
Reliability: (4) Unassignable – data from a secondary literature source
(28)

TERRESTRIAL ORGANISMS

4.6.1 Toxicity to Soil Dwelling Organisms

Type: artificial soil
Species: Eisenia fetida (Worm (Annelida), soil dwelling)
Endpoint: mortality
Exposure period: 14 day
Unit: mg/kg soil dw
NOEC: 225
LC0: 112.5
LC50: 540
LC100: 1800
Method: OECD Guide-line 207 "Earthworm, Acute Toxcity Test"
Year: 1984 GLP: yes
Test substance:
Source: UCB CHEMICALS BRUSSELS
Test substance: Thiram technical (99 % purity)
Reliability: (1) Valid without restriction – Guideline study
(38)

4.8 Biotransformation and Kinetics

Type: plant
Method: 14C-Thiram was applied one time on apples at the 2 cm diameter development stage (rate : 29.5 kg a.i. /ha) Fruits were collected at day 0, 14, 28, 56 and 101 (harvest) after application.

Residues in the fruits were evaluated after washing.
Findings :
- No Thiram (parent) residue was detected in treated fruits except on day 0 as traces.
- Some radioactivity was penetrating the treated fruits. However, it has been established that most of the residues were present as natural products (so, they entered the carbon pool). A portion of the radioactivity (5-7 %) in apples was also associated with CS2 to form the so-called"CS2 generators".

Source: UCB CHEMICALS BRUSSELS
Reliability: (1) Valid without restriction
(39)

5. Toxicity

5.1 Acute Toxicity

5.1.1 Acute Oral Toxicity

Type:	LD50
Species:	rat
Strain:	Sprague-Dawley Albino
Sex:	Male and female
Number of Animals:	20
Vehicle:	Corn oil, 10.0% suspension
Doses:	631, 794, 1000 and 1260 mg/kg bw
Value:	1080 mg/kg bw
Method:	other: Acute LD50 by Single Oral Dose, Younger Laboratories
Year:	1973 GLP: No data
Test substance:	As prescribed by 1.1-1.4, purity 97% minimum
Remark:	Male and female rats (5 animals/dose level)were administered the test substance, as a 10% suspension in corn oil, via oral gavage. Males ranged in weight from 225-245 grams; females were 210-220 grams. Clinical signs of toxicity included reduced appetite and activity (three to seven days in survivors) followed by increasing weakness, collapse and death. Findings from the gross autopsy on decedents were hemorrhagic lungs, liver discoloration and acute gastro-intestinal inflammation. After a 10-day observation period, the survivors were sacrificed. Areas of lung congestion and slight liver discoloration were noted in some of these animals. 95% confidence limits: 1030-1130 mg/kg
Source:	Monsanto Y-73-216
Reliability:	(1) Valid without restriction

(40)

Type:	LD50
Species:	rat
Strain:	
Sex:	
Number of Animals:	
Vehicle:	
Value:	ca. 1800 mg/kg bw
Method:	other: EPA/FIFRA u 81-1
Year:	1982 GLP: yes
Test substance:	other TS: Thiram grade 99-100 %
Remark:	Clinical signs: body weight loss, apathy, reduced locomotive activity, laboured breathing, ungroomed appearance, reduced fecal excretion, (half) closed and moist eyes, tremors of the head.
Source:	UCB CHEMICALS BRUSSELS
Reliability:	(2) Valid with restrictions - meets generally accepted Scientific method but description lacks detail

(41)

Type:	LD50
Species:	rat
Strain:	
Sex:	
Number of Animals:	

Vehicle:
Value: 2600 mg/kg bw
Method: other
Year: 1985 GLP: yes
Test substance: as prescribed by 1.1 - 1.4
Remark: BG Chemie, Toxicological Evaluations 3 reports several acute oral LD50 values (rat) in the range of 800-4000 mg/kg. The composition of the tested material however is not given. Study was carried out in conformity with EPA Guideline 81-1.
Source: Akzo Nobel Chemicals GmbH Dueren
Reliability: (4) Unassignable – data from a secondary literature source

(42)

Type: LD50
Species: rat
Strain:
Sex:
Number of Animals:
Vehicle:
Value: 1112 mg/kg bw
Method:
Year: GLP:
Test substance: as prescribed by 1.1 - 1.4
Source: Akzo Nobel Chemicals GmbH Dueren
Reliability: (4) Unassignable – data from a secondary literature source

(43)

Type: LD50
Species: rat
Strain:
Sex:
Number of Animals:
Vehicle:
Value: 1278 mg/kg bw
Method:
Year: GLP:
Test substance: as prescribed by 1.1 - 1.4
Remark: Unfasted rats were used.
Source: Akzo Nobel Chemicals GmbH Dueren
Reliability: (2) Valid with restrictions – meets generally accepted Scientific method but description lacks detail

(44)

5.1.2 Acute Inhalation Toxicity

Type: LC50
Species: rat
Strain:
Sex:
Number of Animals:
Vehicle:
Exposure time: 4 hour(s)
Value: ca. 4.42 mg/l
Method: other: EPA/FIFRA u 81-3
Year: 1982 GLP: yes
Test substance: other TS: Thiram technical (99.5 % purity)
Remark: Clinical signs; activity decrease, constricted pupils,gasping, lacrimation, nasal discharge,

pilo-erection, polyuria, ptosis, salivation.
Source: UCB CHEMICALS BRUSSELS
Reliability: (2) Valid with restrictions – meets generally accepted Scientific method but description lacks detail

(45)

Type: LC50
Species: rat
Strain:
Sex:
Number of Animals:
Vehicle:
Exposure time: 4 hour(s)
Value: > .1 mg/l
Method: other
Year: 1985 GLP: yes
Test substance: as prescribed by 1.1 - 1.4
Remark: No deaths, some labored breathing, subsided in 16 hrs. No gross pathological abnormalities. Slight to severe inflammation in the lungs.
Note: A large difference in nominal (6.34 mg/l) and measured concentration (0.1 mg/l).
Nose only exposure
Source: Akzo Nobel Chemicals GmbH Dueren
Reliability: (2) Valid with restrictions – meets generally accepted Scientific method but description lacks detail

(46)

Type: LC50
Species: rat
Strain:
Sex:
Number of Animals:
Vehicle:
Exposure time: 4 hour(s)
Value: 4.42 mg/l
Method: other
Year: 1987 GLP: no data
Test substance: as prescribed by 1.1 - 1.4
Remark: Whole body exposure
Source: Akzo Nobel Chemicals GmbH Dueren
Reliability: (2) Valid with restrictions – meets generally accepted Scientific method but description lacks detail

(47)

Type: LC50
Species: rat
Strain:
Sex:
Number of Animals:
Vehicle:
Exposure time: 4 hour(s)
Value: .5 mg/l
Method: other
Year: 1986 GLP: no data
Test substance: no data
Source: Akzo Nobel Chemicals GmbH Dueren
Reliability: (4) Unassignable – data from a secondary literature source

(48)

Type:	LC50
Species:	rat
Strain:	
Sex:	
Number of Animals:	
Vehicle:	
Exposure time:	4 hour(s)
Value:	> 2.63 mg/l
Method:	other
Year:	GLP: no data
Test substance:	no data
Source:	Akzo Nobel Chemicals GmbH Dueren
Reliability:	(4) Unassignable – data from a secondary literature source (49)

Type:	LC50
Species:	rat
Strain:	
Sex:	
Number of Animals:	
Vehicle:	
Exposure time:	4 hour(s)
Value:	> 6.225 mg/l
Method:	
Year:	GLP:
Test substance:	as prescribed by 1.1 - 1.4
Remark:	6.225 mg/l was the maximal attainable dust concentration which could be generated. At this concentration no deaths occurred.
Source:	Akzo Nobel Chemicals GmbH Dueren
Reliability:	(4) Unassignable – data from a secondary literature source (43)

5.1.3 Acute Dermal Toxicity

Type:	LD50
Species:	rabbit
Strain:	New Zealand Albino
Sex:	Male and female
Number of Animals:	3
Vehicle:	Corn oil, 40.0% suspension
Doses:	5010 and 7940 mg/kg bw
Value:	>7940 mg/kg bw
Method:	other: Acute LD50 by Single Dermal Dose, Younger Laboratories
Year:	1973 GLP: No data
Test substance:	As prescribed by 1.1-1.4, purity 97% minimum
Remarks:	The test compound, as a 40% suspension in corn oil, was applied to the shaved skin of two male (weight 2.4 and 2.5 kg) and one female rabbit (weight 2.2 kg) for 24 hours. Clinical signs of toxicity were reduced appetite and activity for four to seven days. All animals survived but lost weight during the study. After a 14-day observation period, the animals were sacrificed. Slight lung congestion and slight discoloration of the liver and kidneys were noted in all animals.
Source:	Monsanto Y-73-216, 1973
Reliability:	(1) valid without restriction (40)

Type: LD50
Species: rat
Strain:
Sex:
Number of Animals:
Vehicle:
Value: > 2000 mg/kg bw
Method: other
Year: 1985 GLP: yes
Test substance: as prescribed by 1.1 - 1.4
Remark: Study according to EPA-540/9-82-025, paragraph 81-2.
Source: Akzo Nobel Chemicals GmbH Dueren
Reliability: (2) Valid with restrictions – meets generally accepted Scientific method but description lacks detail

(42)

Type: LD50
Species: rat
Strain:
Sex:
Number of Animals:
Vehicle:
Value: > 5000 mg/kg bw
Method: other
Year: 1990 GLP: no data
Test substance: no data
Source: Akzo Nobel Chemicals GmbH Dueren
Reliability: (4) Unassignable – data from a secondary literature source

(50)

Type: LD50
Species: rat
Strain:
Sex:
Number of Animals:
Vehicle:
Value: > 5000 mg/kg bw
Method:
Year: GLP:
Test substance: as prescribed by 1.1 - 1.4
Source: Akzo Nobel Chemicals GmbH Dueren
Reliability: (2) Valid with restrictions – meets generally accepted Scientific method but description lacks detail

(43)

Type: LD50
Species: rabbit
Strain:
Sex:
Number of Animals:
Vehicle:
Value: >= 2000 mg/kg bw
Method: other: EPA/FIFRA u 81-2
Year: 1982 GLP: yes
Test substance: other TS: Thiram technical (98.8 % purity)
Remark: Clinical signs : slight to moderate erythema.
Macroscopic examination : no findings
Source: UCB CHEMICALS BRUSSELS

Reliability: (2) Valid with restrictions – meets generally accepted Scientific method but description lacks detail

Type: LD50
Species: rabbit
Strain:
Sex:
Number of Animals:
Vehicle:
Value: >= 2000 mg/kg bw
Method: other: EPA/FIFRA par. 81-2
Year: 1982 GLP: yes
Test substance: other TS: Thiram technical (98.8% purity)
Remark: Clinical signs : slight to moderate erythema.
Macroscopic examination : no findings.
Source: UCB-Chemicals Gent
Reliability: (2) Valid with restrictions – meets generally accepted Scientific method but description lacks detail

(51)

5.2 Corrosiveness and Irritation

5.2.1 Skin Irritation

Species: rabbit
Concentration:
Exposure:
Exposure Time:
Number of Animals:
PDII:
Result: not irritating
EC classificat.: not irritating
Method: other: EPA/FIFRA u 81-5
Year: 1982 GLP: yes
Test substance: other TS: Thiram technical (98.8 % purity)
Source: UCB CHEMICALS BRUSSELS
Reliability: (2) Valid with restrictions – meets generally accepted Scientific method but description lacks detail

(52)

Species: rabbit
Concentration:
Exposure:
Exposure Time:
Number of Animals:
PDII:
Result: not irritating
EC classificat.: not irritating
Method: other
Year: 1985 GLP: yes
Test substance: as prescribed by 1.1 - 1.4
Remark: 4 hour application time.
Study according to EPA Guideline EPA-540/9-82-025, paragraph 81-5.
Source: Akzo Nobel Chemicals GmbH Dueren
Reliability: (2) Valid with restrictions – meets generally accepted Scientific method but description lacks detail

(53)

Species: rabbit
Concentration:

Exposure:
Exposure Time:
Number of
Animals:
PDII:
Result: moderately irritating
EC classificat.: not irritating
Method: other
Year: 1982 GLP: no
Test substance: as prescribed by 1.1 - 1.4
Remark: 24 hour application time
Source: Akzo Nobel Chemicals GmbH Dueren
Reliability: (2) Valid with restrictions - meets generally accepted Scientific method but description lacks detail

(54)

5.2.2 Eye Irritation

Species: rabbit
Concentration:
Dose:
Exposure Time:
Comment:
Number of
Animals:
Result: irritating
EC classificat.: irritating
Method: other: EPA/FIFRA u 81-4
Year: 1982 GLP: yes
Test substance: other TS: Thiram technical (98.8 % purity)
Remark: Irritation symptoms were reversible within 15 days after dosing.
Source: UCB CHEMICALS BRUSSELS
Reliability: (2) Valid with restrictions - meets generally accepted Scientific method but description lacks detail

(55)

Species: rabbit
Concentration:
Dose:
Exposure Time:
Comment:
Number of
Animals:
Result: not irritating
EC classificat.: not irritating
Method: other
Year: 1985 GLP: yes
Test substance: as prescribed by 1.1 - 1.4
Source: Akzo Nobel Chemicals GmbH Dueren
Reliability: (2) Valid with restrictions - meets generally accepted Scientific method but description lacks detail

(56)

5.3 Sensitization

Type: Guinea pig maximization test
Species: guinea pig
Number of Animals:
Vehicle:
Result: ambiguous
Classification:
Method: other
Year: 1982 GLP: yes
Test substance: as prescribed by 1.1 - 1.4
Remark: Study according to Magnusson and Kligman, 1970. At 10% challenge treatment: 3 out of 10 animals showed a positive reponse. At 5% challenge concentration 1 out of 10 animals showed a positive response.
Source: Akzo Nobel Chemicals GmbH Dueren
Reliability: (2) Valid with restrictions – meets generally accepted Scientific method but description lacks detail

(57)

Type: Split adjuvant test
Species: guinea pig
Number of Animals:
Vehicle:
Result: sensitizing
Classification: sensitizing
Method: OECD Guide-line 406 "Skin Sensitization"
Year: 1985 GLP: yes
Test substance: as prescribed by 1.1 - 1.4
Remark: 40% positive reponse. Moderate sensitizer.
Source: Akzo Nobel Chemicals GmbH Dueren
Reliability: (1) Valid without restriction – Guideline study

(58)

Type: Split adjuvant test
Species: guinea pig
Number of Animals:
Vehicle:
Result: sensitizing
Classification: sensitizing
Method: other: EPA/FIFRA par. 81-6
Year: 1982 GLP: yes
Test substance: other TS: Thiram 99-100% grade
Remark: A moderate sensitizer (grade III) following Klingman (1966).
Source: UCB-Chemicals Gent
Reliability: (2) Valid with restrictions – meets generally accepted Scientific method but description lacks detail

(59)

5.4 Repeated Dose Toxicity

Species: rat Sex: male/female
Strain: other
Route of admin.: oral feed
Exposure period: 90 days
Frequency of treatment: continuous
Post. obs. period: not applicable

Doses: 50, 500 and 1000 ppm nominal
Control Group: yes
NOAEL: ca. 2.5 mg/kg bw
Method: other: EPA/FIFRA u 82-1
Year: 1982 GLP: yes
Test substance: other TS: Thiram technical (99.4 % purity)
Result: Body weights, cumulative body-weight gains, and food consumption were significantly reduced throughout the study for both sexes at 500 and 1000 ppm.

Changes in clinical chemistry and haematological parameters occurred at dose levels of 500 and 1000 ppm. The changes considered to be treatment-related were reduced red blood cell count, haemoglobin and haematocrit in females ; increased MCV and MCH in both sexes; increased white blood cell, corrected white blood cell, absolute neutrophil, absolute lymphocyte and absolute monocyte counts in females; reduced total protein and glucose in both sexes; reduced albumin and increased urea nitrogen and chloride in females.

At 500 and 1000 ppm animals a tendency to reduced terminal body-weights with correspondingly reduced absolute organ weights and increased organ to body-weight ratios were observed.

Macroscopically, the non-glandular stomach in some animal showed areas of erosion and the mesenteric lymph nodes were diffusely red or mottled. Microscopically, the mucosa of the nonglandular stomach had focal areas of erosion/ulceration, mucosal hyperplasia, or both, accompanied by some submucosal inflammation and edema. These changes appeared to be treatment-related. The mesenteric lymph nodes were frequently congested but otherwise normal.
Source: UCB CHEMICALS BRUSSELS
Reliability: (1) Valid without restriction

(60)

Species: rat Sex: male
Strain: other: Charles River
Route of admin.: oral feed
Exposure period: 13 weeks
Frequency of treatment: daily
Post. obs. period:
Doses: 0, 0.05, 0.1 or 0.25 %
Control Group: yes
Method:
Year: GLP:
Test substance:
Remark: At all dose groups significant reductions in body weight and feed consumption were observed. In the medium dose group a slight increase in blood urea was observed, and in the high dose group there was an increase in the activity of aspartate aminotransferase and alanine amino transferase and moderate tubular degeneration of the testes.
Source: Akzo Nobel Chemicals GmbH Dueren
Reliability: (4) Unassignable – data from a secondary literature source

(61)

Species: rat Sex: male/female
Strain: Fischer 344/DuCrj
Route of admin.: oral feed
Exposure period: 13 weeks
Frequency of treatment: daily
Post. obs. period:
Doses: 0, 0.015, 0.03 or 0.06 %
Control Group: yes
NOAEL: .03 %
Method: other
Year: GLP: no data
Test substance:
Remark: Increased liver enzyme (LDH, SGOT, SGPT) levels were noted in the high exposure animals of both sexes, but females only showed slight histopatholigical changes in the lever.
Source: Akzo Nobel Chemicals GmbH Dueren
Reliability: (4) Unassignable – data from a secondary literature source (62)

5.5 Genetic Toxicity 'in Vitro'

Type: Ames test
System of testing: Salmonella typhimurium strains TA1537, TA97, TA1538 TA98, TA1535 and TA100.
Concentration: 1-50 ug/plate
Cytotoxic Conc.:
Metabolic activation: with and without
Result: positive
Method: other
Year: 1982 GLP: no
Test substance: other TS
Remark: The majority of literature and company reports on Ames Salmonella assays have shown mutagenic activity.
References:
Lijinsky, W. (1984). Induction of tumors of the nasal cavity in rats by concurrent feeding of thiram and sodium nitrite. J. Toxicol. Environ. Health. 13, 609-614.
Monsanto study BO-76-277.
Uniroyal study (1982).
Goodyear study (1989). Only positive in TA1535 with S9-mix.
Moriya, M. et al. (1983). Further mutagenicity studies on pesticides in bacterial reversion assay systems. Mut. Res., 116, 185-216.
Rannug, A. et al. (1984). Genotoxic effects of additives in synthetic elastomers with special consideration to the mechanism of action of thiurams and dithiocarbamates. prog. Clin. Bio. Res. 141, 407-419.
Rannug, A. and Rannug. U. (1984). Enzyme inhibition as possible mechanism of the mutagenicity of thiocarbamic acid derivatives in Salmonella typhimurium. Chem. Biol. Interact. 49, 329-340.
Hedenstedt, A. et al. (1979). Mutagenicity and metabolism studies on 12 thiuram and dithiocarbamate compounds used as accelerators in the Swedish rubber industry. Mut. Res. 68, 313-325.
Zdzienicka, M. et al. (1979). Mutagenic activity of thiram in Ames tester strains of Salmonella typhimurium. Mut. Res. 68, 9-13.

Source: Akzo Nobel Chemicals GmbH Dueren
Test substance: Test substance stated to be 98% A.I. material
Reliability: (4) Unassignable – data from secondary literature sources

(63)

Type: Cytogenetic assay
System of testing: Chinese Hamster Ovary cells
Concentration: 0.56, 1.8 and 5.6 ug/ml (without S-9 mix), 1.8, 5.6 and 18 ug/ml (with S-9 mix)
Cytotoxic Conc.:
Metabolic activation: with and without
Result: positive
Method: OECD Guide-line 473 "Genetic Toxicology: In vitro Mammalian Cytogenetic Test"
Year: 1985 GLP: yes
Test substance: as prescribed by 1.1 - 1.4
Remark: At 10 hour harvest time 6 fold increase in aberration frequency (chromatid type) both with and without activation. No assessment was made for potential cell cycle delay. Dose levels may have been too high. No check for pH or osmolality.
Source: Akzo Nobel Chemicals GmbH Dueren
Reliability: (1) Valid without restrictions – Guideline study

(64)

Type: Cytogenetic assay
System of testing: Chinese Hamster Ovary cells
Concentration: 0.003-0.023 ug/ml without and 0.2-1.5 ug/ml with activation
Cytotoxic Conc.:
Metabolic activation: with and without
Result: negative
Method: other
Year: 1987 GLP: yes
Test substance: as prescribed by 1.1 - 1.4
Remark: Metabolic activation: Aroclor 1254 induced rat liver S-9 mix.
Harvest times: 16 hours (with S-9 mix) (because a cell cycle delay was observed, the cells were harvested at 16 hrs., in order to assure that all cells were evaluated during the first division methaphase). 10 hours (without S-9 mix)
Source: Akzo Nobel Chemicals GmbH Dueren
Reliability: (2) Valid with restrictions – meets generally accepted Scientific method but description lacks detail

(65)

Type: Cytogenetic assay
System of testing: L5178Y mouse lymphoma cells
Concentration: 1.8 - 20 ug/ml
Cytotoxic Conc.:
Metabolic activation: with and without
Result: ambiguous
Method: other
Year: 1982 GLP: no
Test substance: other TS
Remark: Two other studies showing weak activity on L5178Y mouse lymphoma cells are reported.

Monsanto study BIO-77-324
Paik, S.G and Lee, S.Y. (1977). Genetic effects of pesticides in the maamalian cells. II. Mutagenesis in L5178Y cells and DNA repair induction. Tongmul. Hakhoe. Chi, 20, 159-168.
Unusual cell type
Cytotoxicity not well determined.
2 Hour exposure: Cytogenetic effects were observed at cytotoxic concentrations.
At 24 hour exposure to considerably lower concentrations did not show an increase in chromosomal aberrations.

Source: Akzo Nobel Chemicals GmbH Dueren
Test substance: 98% A.I. material was used.
Reliability: (2) Valid with restrictions - meets generally accepted Scientific method but description lacks detail

(66)

Type: Cytogenetic assay
System of testing: Chinese hamster ovary cells (CHO)
Concentration: 0.003, 0.006, 0.012, 0.023, 0.2, 0.4, 0.8, 1.5 ug/plate
Cytotoxic Conc.:
Metabolic activation: with and without
Result: negative
Method: other: EPA/FIFRA par. 84-2
Year: 1982 GLP: yes
Test substance: other TS: Thiram technical (99.8% purity)
Source: UCB-Chemicals Gent
Reliability: (1) Valid without restriction

(67)

Type: DNA damage and repair assay
System of testing: Monolayer cultures of rat (Sprague Dawley) hepatocytes
Concentration: 0.005 ug/ml up to 1 mg/ml
Cytotoxic Conc.:
Metabolic activation: without
Result: negative
Method: other: acc. to Williams, G.M. 1977
Year: GLP: yes
Test substance: as prescribed by 1.1 - 1.4
Remark: At a level of 0.02 mg/ml and higher the test material was toxic to the hepatocytes. At lower concentrations no DNA repair was observed.
Source: Akzo Nobel Chemicals GmbH Dueren
Reliability: (2) Valid with restrictions - meets generally accepted Scientific method but description lacks detail

(68)

Type: HGPRT assay
System of testing:
Concentration:
Cytotoxic Conc.:
Metabolic activation:
Result:
Method:
Year: GLP:
Test substance:

Remark: One positive and one negative finding have been reported for the HGPRT locus in CHO cells.
Source: Akzo Nobel Chemicals GmbH Dueren
Reliability: (4) Unassignable - data from a secondary literature source

(69)

Type: Mammalian cell gene mutation assay
System of testing: V79 Chinese Hamster Cells
Concentration: 1 to 56 ug/ml culture medium
Cytotoxic Conc.:
Metabolic activation: with and without
Result: negative
Method: OECD Guide-line 476 "Genetic Toxicology: In vitro Mammalian Cell Gene Mutation Tests"
Year: 1986 GLP: yes
Test substance: as prescribed by 1.1 - 1.4
Remark: The test material was tested up to cytotoxic concentrations, without a significant increase in mutant frequency at any test concentration.
Confirmed with an independent repeat.
Source: Akzo Nobel Chemicals GmbH Dueren
Reliability: (1) Valid without restriction - Guideline study

(70)

Type: Mammalian cell gene mutation assay
System of testing: L5178Y mouse lyphoma cells
Concentration: 2.4 up to 20 ug/ml
Cytotoxic Conc.:
Metabolic activation: with and without
Result: ambiguous
Method: other
Year: 1982 GLP: no
Test substance: other TS
Remark: Method according to Clive, D. Mutation Research, 31, 17-29, 1975.
Results without metabolic activation: Cannot be evaluated because less than 10% cell survival in 2 of the 3 dosages. Concentrations used are too high.
Results with metabolic activation: a dose related increase in mutation frequency at the HGPRT-locus, no effect at the TK-locus
Source: Akzo Nobel Chemicals GmbH Dueren
Test substance: >98% A.I. material is used
Reliability: (2) Valid with restrictions - meets generally accepted Scientific method but description lacks detail

(71)

Type: Mammalian cell gene mutation assay
System of testing: V79 Chinese hamster cells (checks on HGPRT locus)
Concentration: 1, 3.3, 5.6, 10, 18, 33, 56 ug/ml
Cytotoxic Conc.:
Metabolic activation: with and without
Result: negative
Method: other: EPA/FIFRA par. 84-2
Year: 1982 GLP: yes
Test substance: other TS: Thiram 99-100% grade

Source: UCB-Chemicals Gent
Reliability: (1) Valid without restriction

(72)

Type: Salmonella typhimurium reverse mutation assay
System of testing: S. Typhimurium strains TA1537, TA1538, TA98, TA1535 and TA100
Concentration: 1.0, 3.3, 10.0, 33.3, 66.6, 100.0, 333.3, 666.6, 1000.0 ug/plate
Cytotoxic Conc.:
Metabolic activation: with and without
Result: positive
Method: other: EPA/FIFRA par. 84-2
Year: 1982 GLP: yes
Test substance: other TS: Thiram technical (98.7% purity)
Source: UCB-Chemicals Gent
Reliability: (2) Valid with restrictions - meets generally accepted Scientific method but description lacks detail

(73)

Type: Unscheduled DNA synthesis
System of testing: primary culture of rat hepatocytes
Concentration: 0.03 up to 10 ug/ml
Cytotoxic Conc.:
Metabolic activation: without
Result: negative
Method: other
Year: 1985 GLP: yes
Test substance: as prescribed by 1.1 - 1.4
Remark: Independent repeat.
Source: Akzo Nobel Chemicals GmbH Dueren
Reliability: (2) Valid with restrictions - meets generally accepted Scientific method but description lacks detail

(74)

Type: Unscheduled DNA synthesis
System of testing: primary culture of rat hepatocytes
Concentration: 0.03, 0.10, 0.3, 1.0, 3.0, 10.0 ug/plate
Cytotoxic Conc.:
Metabolic activation: without
Result: negative
Method: other: EPA/FIFRA par. 84-2
Year: 1982 GLP: yes
Test substance: other TS: Thiram 99-100% grade
Source: UCB-Chemicals Gent
Reliability: (2) Valid with restrictions - meets generally accepted Scientific method but description lacks detail

(75)

5.6 Genetic Toxicity 'in Vivo'

Type: Mammalian germ cell cytogenetic assay
Species: mouse Sex: male
Strain: NMRI
Route of admin.: gavage
Exposure period: up to 48 hours after treatment
Doses: 0, 75, 250 and 750 mg/kg bw
Result:

Method: Directive 87/302/EEC, part B, p. 79 "Mutagenicity: - In vivo mammalian germ-cell cytogenetics"
Year: 1987 GLP: yes
Test substance: other TS: Thiram technical (99.7 % purity)
Result: negative
Source: UCB CHEMICALS BRUSSELS
Reliability: (2) Valid with restrictions – meets generally accepted Scientific method but description lacks detail

(76)

Type: Micronucleus assay
Species: mouse Sex: male/female
Strain: CD-1
Route of admin.: i.p.
Exposure period: 24, 48 and 72 hours after treatment
Doses: 377, 189 and 38 mg/kg
Result:
Method: other
Year: 1987 GLP: yes
Test substance: as prescribed by 1.1 - 1.4
Remark: No increase in micronuclei in male or female mice was found.
Source: Akzo Nobel Chemicals GmbH Dueren
Reliability: (2) Valid with restrictions – meets generally accepted Scientific method but description lacks detail

(77)

Type: Micronucleus assay
Species: mouse Sex: male/female
Strain: CD-1
Route of admin.: i.p.
Exposure period: up to 72 hours after treatment
Doses: 38, 189 and 377 mg/kg bw; no positive controls
Result:
Method: other: EPA/FIFRA par. 84-2
Year: 1982 GLP: yes
Test substance: other TS: Thiram technical (99.8% purity)
Result: negative
Source: UCB-Chemicals Gent
Reliability: (2) Valid with restrictions – meets generally accepted Scientific method but description lacks detail

(78)

Type: Somatic mutation assay
Species: mouse Sex: male/female
Strain: other: DBA, NMRI
Route of admin.: other: gavage (one application on day 9 of pregnancy)
Exposure period: from day 9 of pregnancy
Doses: 0, 75, 750 mg/kg bw (in females)
Result:
Method: OECD Guide-line 484 "Genetic Toxicology: Mouse Spot Test"
Year: 1986 GLP: yes
Test substance: other TS: Thiram technical (98.7 % purity)
Result: negative with test substance, positive with positive controls
Source: UCB CHEMICALS BRUSSELS
Reliability: (2) Valid with restrictions – meets generally accepted Scientific method but description lacks detail

(79)

5.7 Carcinogenicity

Species: rat Sex: male/female
Strain: CD-1
Route of admin.: oral feed
Exposure period: 104 weeks
Frequency of treatment: continuous
Post. obs. period: after treatment : nil
Doses: 0, 30, 150, 300 ppm in the diet; number of rats : 60/sex/group
Result:
Control Group: yes, concurrent no treatment
Method: other: EPA/FIFRA u 83-2 (a)
Year: 1982 GLP: yes
Test substance: other TS: Thiram technical (97.5 % purity)
Result:
- Antemortem possible material-related observations : swollen nose, soft feces, opaque eye in male rats; soft feces in female rats
- Likely no test material-related ophtalmic lesions were noted
- Survival statistically significantly higher for males given 300 ppm
- Mean body weights and cumulative body weight gain were statistically significantly lower than those of the controls at 150 ppm and 300 ppm, but not at 30 ppm at week 104
- No consistent effect on food consumption at any level in males, no statistically significant effect on food consumption in females
- Blood picture affected at 150 ppm and 300 ppm in females
- No significantly increased incidence of carcinomas or adenomas in liver, thyroid or any other organ was noted at any of the dose levels tested with respect to the controls. However a statistically significant positive trend for hepatocellular and thyroid C-cell adenomas in both sexes, as well as for bile duct hyperplasia in females was evidenced. Extramedullary hematopoiesis in the liver of males at the medium and high dose, and of females at the high dose as well as steatosis of the pancreas in both sexes was noted
- No antemortem observations and no histopathological findings suggested test material-related neurotoxicity
- NOEL : 30 ppm corresponding to 1.46 (1.02 - 3.25) mg/kg b.w./day in males, and 1.80 (1.30 - 3.31) mg/kg b.w./day in females

Source: UCB CHEMICALS BRUSSELS
Reliability: (1) Valid without restriction

(80)

Species: rat Sex: male/female
Strain: Fischer 344
Route of admin.: oral feed
Exposure period: 2 year
Frequency of treatment: daily
Post. obs. period:
Doses: 500 ppm (0.05% in the feed)
Result:

Control Group: yes, concurrent no treatment
Method: other
Year: 1984 GLP: no data
Test substance: no data
Remark: Study from the National Cancer Institute.
In animals treated with the test substance alone no increase in tumours was noted.
When the animals were fed 500 ppm test substance and 2000 ppm sodium nitrite in their feed for 2 years, tumors of the nasal cavity were found.
Source: Akzo Nobel Chemicals GmbH Dueren
Reliability: (2) Valid with restrictions - meets generally accepted Scientific method but description lacks detail

(81)

Species: rat Sex: male/female
Strain: Fischer 344
Route of admin.: oral feed
Exposure period: 104 weeks
Frequency of treatment: daily
Post. obs. period: 8 weeks
Doses: 0, 0.05 and 0.1% in the diet
Result:
Control Group: yes, concurrent no treatment
Method: other
Year: 1988 GLP: no data
Test substance: no data
Remark: No significant lesions or tumor induction attributable to the treatment were observed. Not carcinogenic.
Source: Akzo Nobel Chemicals GmbH Dueren
Reliability: (4) Unassignable - data from a secondary literature source

(82)

Species: mouse Sex: male/female
Strain: CD-1
Route of admin.: oral feed
Exposure period: 97 weeks
Frequency of treatment: continuous
Post. obs. period: after treatment : nil
Doses: 0, 15, 150, or 300 ppm (males) and 0, 15, 300, or 600 ppm (females). Number of mice : 50/sex/group
Control Group: no
Method: other: EPA/FIFRA u 83-2 (b)
Year: 1982 GLP: yes
Test substance: other TS: Thiram technical (97.5 % purity)
Result:
- No compound-related oncogenic effects noted up to 300 ppm in males (equal to 50 mg/kg b.w./day), and 600 ppm in females (equal to 112 mg/kg b.w./day)
- No adverse effects on survival, and no indication of neurotoxicity (based on clinical signs) were noted at any test level
- Decrease of body weight, weight gain and food consumption noted at the mid and high dose levels
- No remarkable clinical observations noted (however higher frequencies of sores or reddened areas noted at the high doses)
- Principal clinical haematology findings (decreased

mean erythrocete count, haemoglobin, and haematocrit values) were noted in the 600 ppm females at termination
- No compound-related gross tissue alterations and no organ weight findings were noted
- Histopathology : no evidence of Thiram-induced neoplasia was shown. Further nonneoplastic effects were observed only at the mid and high doses
Other effects : retinal atrophy, intracytoplasmic protein like droplets in the urinary bladder superficial transitional epithelium, and necrosis and suppurative inflammation in the skin at the mid and high doses; hyperkeratosis in the nonglandular stomach of the 300 ppm males, 300 and 600 ppm females; increased pigment in the spleen and decreased pigment in the inner adrenal cortex of the 300 and 600 ppm females
- NOEL for toxic effects was 15 ppm (equal to 3 mg/kg b.w./day)

Source: UCB CHEMICALS BRUSSELS
Reliability: (1) Valid without restriction

(83)

Species: mouse Sex: male/female
Strain: NMRI
Route of admin.: oral feed
Exposure period: 104 weeks
Frequency of treatment: daily
Post. obs. period:
Doses: 30, 100 or 300 ppm
Result:
Control Group: yes
Method:
Year: GLP: no data
Test substance: other TS
Remark: Result: no substance or dose-dependent increase in the number of tumours in treated animals was found compared to the controls. Not carcinogenic.
Source: Akzo Nobel Chemicals GmbH Dueren
Test substance: 99.6% pure material was used.
Reliability: (4) Unassignable – data from a secondary literature source

(84)

Species: Mice Sex:
Strain:
Route of admin.:
Exposure period:
Frequency of treatment:
Post. obs. period:
Doses:
Result:
Control Group:
Method:
Year: GLP:
Test substance:
Remark: Groups of male and female mice were dosed Thiram at 10 mg/kg in gelatin at seven days of age by stomach tube and the same amount (not adjusted for increasing body weight) daily up to four weeks of age. Subsequently, the mice were given

26 mg/kg of diet daily up 78 weeks of age. No sign. increase of tumors of any type were found.

Groups of male and female mice were given single s.c. injections of 46.4 mg/kg thiram in 0.5 percent gelatin on day 28 of life. The animals were observed up to the age of 78 weeks. Tumor incidences were compared to controls and vehicle injected controls. No increase in tumors observed.

Reference: NTIS (1968). Evaluation of carcinogenic , teratogenic and mutagenic activities of selected pesticides and industrial chemicals. National Technical Information Service, 1. Carcinogenic Study, Washington DC, Department of Commerce.

Source: Akzo Nobel Chemicals GmbH Dueren

Reliability: (2) Valid with restrictions – meets generally accepted Scientific method but description lacks detail

(85)

5.8 Toxicity to Reproduction

Type: Two generation study
Species: rat Sex: male/female
Strain: CD-1
Route of admin.: oral feed
Exposure Period: 81 days continuously in F0 animals and 84 days continuously in F1 animals
Frequency of treatment: see above
Premating Exposure Period
male: F0 animals : treatment started at 63 days of age for 81 days (then mating)
female: F1 animals : treatment started at 22 days of age for 84 days (then mating)
Duration of test:
Doses: 0, 30, 60 and 180 ppm in the diet. Number of animals : 26/sex/group
Control Group: yes
Method: other: EPA/FIFRA u 83-4
Year: 1982 GLP: yes
Test substance: other TS: Thiram technical (97.6 % purity)
Result: Parental systemic toxicity :

- No mortalities or antemortem findings noted at any of the dose levels treated.
- Mean maternal b.w. and food consumption reduced :
  * in F0 females at 60 and 180 ppm during F1a gestation, at 180 ppm during F1b and F1c gestations, and the the relevant lactation periods
  * in F1 females at 180 ppm during F2a and F2b gestation and lactation periods
- Mean food consumption reduced in Fo males and females at 60 and 180 ppm
- NOEL : 30 ppm for the F1a mating (equal to 1.5 and 2.3 mg/kg b.w./day in males and females, resp.) 60 ppm for all subsequent matings

Filial systemic toxicity :

- Mean offspring b.w.'s reduced across both generations at 180 ppm
- NOEL : 60 ppm (equal to 3.8 and 5.1 mg/kg b.w./day in males and females, resp.)

Reproductive toxicity :
- Neither the male and female copulatority and fertility indices nor the gestation index were affected by treatment
- NOEL : 180 ppm (equal to 8.9 and 14 mg/kg b.w./day in males and females, resp.)

Developmental toxicity :
- Mean number of stillborn or live births unaffected by treatment in F1 or F2 litters
- Survival indices alike antemortem and necropsy findings unaffected by treatment for the F1 or F2 offspring.
- NOEL : 180 ppm (equal to 8.9 and 14 mg/kg b.w./day in males and females, resp.)

Source: UCB CHEMICALS BRUSSELS
Reliability: (1) Valid without restriction

(86)

Type:
Species: Sex:
Strain:
Route of admin.:
Exposure Period:
Frequency of treatment:
Duration of test:
Doses:
Control Group:
Method:
Year: GLP:
Test substance:
Remark: No effects on reproduction were seen in three generations of rats fed 48 mg/kg/day in the diet (1).
TMTD was administered to rats at 0, 0.05, 0.1, 0.5, 1.0, 5.0 or 25 mg/kg/day for six months. No effects on reproductive activity were reported (2). In a study were females were given 25 mg thiram/kg daily throughout preganancy, symptoms of maternal toxicity were observed, but no effects on reproduction. (2).

Rats were fed diets containing TMTD for 13 weeks prior to mating. Males treated at 132 mg/kg/day in the diet for 13 weeks failed to impregnate females. No effects were observed at 30 or 58 mg/kg/day.
Females rats fed at 30 or 96 mg/kg/day for 13 weekd=ks had reduced numbers of implants and viable embryos (3).

A series of further reproduction toxicity studies are mentioned cited in: BG Chemie, Toxicological evaluation 3, Potential Health Hazards of Existing Chemicals, Springer Verlag. Germany.
Source: Akzo Nobel Chemicals GmbH Dueren
Reliability: (4) Unassignable - data from secondary literature sources

(87)

5.9 Developmental Toxicity/Teratogenicity

Species: rat Sex: female
Strain: CD-1
Route of admin.: gavage
Exposure period: From day 6 to 15 inclusive of gestation

Frequency of treatment: once a day over exposure period
Duration of test: females were sacrificed on day 20 of gestation
Doses: 7.5, 15 and 30 mg/kg b.w./day
Control Group: yes, concurrent no treatment
NOAEL Maternalt.: 7.5 mg/kg bw
NOAEL Teratogen.: 7.5 mg/kg bw
Method: other: EPA/FIFRA u 83-3
Year: 1982 GLP: yes
Test substance: other TS: Thiram technical (99 % purity)

Result:

Dose (mg/kg)	Maternal effects	Litter responses/ foetal evaluation
7.5	Body weight gain marginally reduced during treatment, unaffected thereafter	Placental weight slightly affected; no foetal toxicity
15	Transient, slight loss of b.w. noted up to day 8 p.c. thereafter the b.w. gain was essentially unaffected	Placental weight and foetal weight slightly affected (however remained within background control range); incidence of foetuses with reduced 13th ribs slightly increased However incidence not dose-related.
30	Transient loss of b.w. noted up to day 8 p.c., thereafter the b.w. gain was essentially unaffected	Foetal survival unaffected; foetal placental weiths reduced, incidence of foetuses with reduced 13th ribs slightly increased. However, incidence not dose-related

Source: UCB CHEMICALS BRUSSELS
Reliability: (1) Valid without restriction

(88)

Species: rat Sex: female
Strain: no data
Route of admin.: gavage
Exposure period: day 6 to 15 of gestation
Frequency of treatment: daily
Duration of test:
Doses: 7.5, 15 and 30 mg/kg/day
Control Group: no data specified
NOAEL Maternalt.: > 30 mg/kg bw
NOAEL Teratogen.: 7.5 mg/kg bw
Method: other
Year: 1987 GLP: no data
Test substance: other TS
Remark: Maternal toxicity: A slight temporary decrease in body weight gain was noted during some days of the treatment period.
Fetal effects: decrease in fetal weight and placental

weight at 30 mg/kg/day. Increase in reduced 13th rib size at 15 and 30 mg/kg/day groups, however not dose related.
Source: Akzo Nobel Chemicals GmbH Dueren
Test substance: 99.8 % A.I. Test substance
Reliability: (2) Valid with restrictions – meets generally accepted Scientific method but description lacks detail
(89)

Species: rat Sex: female
Strain: no data
Route of admin.: gavage
Exposure period: day 6-15 of gestation.
Frequency of treatment:
Duration of test:
Doses:
Control Group:
NOAEL Teratogen.: 90 mg/kg bw
Method:
Year: GLP: no data
Test substance: no data
Remark: No teratogenic effects were noted at 90 mg/kg/day. At 40 and 90 mg/kg/day reduced maternal weight gain and fetal body weight reductions were noted.
In the same article a study on mice is reported. Results: mice treated at 100 or 300 TMTD/kg on days 5 through 14 of gestation did not demonstrate embryotoxic or teratogenic effects.
Source: Akzo Nobel Chemicals GmbH Dueren
Reliability: (4) Unassignable – data from a secondary literature source
(90)

Species: mouse Sex: female
Strain: other: NMRI or SW
Route of admin.: gavage
Exposure period: day 6-17 of gestation
Frequency of treatment:
Duration of test: day 6-17 of gestation
Doses: 5-30 mg/day
Control Group:
NOAEL Teratogen.: 250 mg/kg bw
Method:
Year: GLP: no data
Test substance: no data
Source: Akzo Nobel Chemicals GmbH Dueren
Reliability: (4) Unassignable – data from a secondary literature source
(91)

Species: rabbit Sex: female
Strain: New Zealand white
Route of admin.: gavage
Exposure period: from day 6 to 19 inclusive of gestation
Frequency of treatment: once a day over exposure period
Duration of test: females were sacrificed on day 29 of gestation
Doses: 0, 1.0, 2.5 and 5.0 mg/kg b.w./day
Control Group: no
NOAEL Maternalt.: 5 mg/kg bw
NOAEL Teratogen.: 5 mg/kg bw
Method: other: EPA/FIFRA u 83-3
Year: 1982 GLP: yes

Test substance: other TS: Thiram technical (99.5 % purity)

Result:

Dose (mg/kg)	Maternal effects	Litter responses/ foetal evaluation
1	General condition and b.w. performance unaffected	
2.5	General condition and b.w. performance unaffected	Litter parameters, survival, growth and morphological development in utero unaffected
5	General condition unaffected; b.w. performance slightly reduced	

Source: UCB CHEMICALS BRUSSELS
Reliability: (1) Valid without restriction

(92)

Species: rabbit Sex: female
Strain: no data
Route of admin.: gavage
Exposure period: day 6 -19 of gestation
Frequency of treatment: once daily
Duration of test:
Doses: 1, 2.5 and 5 mg/kg/day
Control Group: no data specified
NOAEL Maternalt.: 1 mg/kg bw
NOAEL Teratogen.: > 5 mg/kg bw
Method: other
Year: 1987 GLP: no data
Test substance: other TS
Remark: At 5 mg/kg/day dose level the only effect noted was reduced body weight gain.
Source: Akzo Nobel Chemicals GmbH Dueren
Test substance: 99.7 % A.I. Material
Reliability: (2) Valid with restrictions - meets generally accepted Scientific method but description lacks detail

(93)

Species: hamster Sex: female
Strain:
Route of admin.: oral unspecified
Exposure period: day 7-8 of gestation
Frequency of treatment:
Duration of test:
Doses: 125, 250 or 500 mg/kg
Control Group:
Method:
Year: GLP: no data
Test substance: no data
Remark: At 125 mg/kg, a slight increase in percent of fetuses with terata were noted. At 250 mg/kg and above, fetal mortality and percentage of fetuses with terata were notably increased. Note: high dosing regime.
Source: Akzo Nobel Chemicals GmbH Dueren
Reliability: (4) Unassignable - data from a secondary literature source

(94)

5.10 Other Relevant Information

Type: Metabolism
Remark: Rats were fed a single dose of 14 C-Thiram (2 mg/kg) following administration of unlabelled Thiram at 2 mg/kg for 14 days, then were sacrificed at 96 hours following dosing.

Mean 14C recovery : 85 % (males), 93 % (females)
Absorption : >= 83 % of the dose

Distribution of radioactivity :
- in urine (ca. 35-40 %), feces (ca. 2-5%), expired air (ca.47-48 %) and tissues (ca. 2-3 % left after four days)
- tissues : highest concentrations in liver, blood cells and kidneys.

Source: UCB CHEMICALS BRUSSELS
Reliability: (1) Valid without restriction

(95)

Type: Neurotoxicity
Remark: Type : Neurotoxicity (90-day study)
Results :
Mortality : no incidence
500 ppm : body weight and food consumption depressed.
Neurotoxicity findings (through FOB, motor activity, neuropathology) : no consistent evidence of neurotoxicity shown overall (however, FOB affected slightly)
125 ppm : adverse effects on body weight, food consumption. However, less severe than with 500 ppm
Neurotoxicity : no findings noted
30 ppm : no toxic effects any kind

NOEL : (neurotoxicity) : 125 ppm
NOEL : (adult toxicity) : 30 ppm

Method : EPA/FIFRA u 82-5
Year : 1991
GLP : yes

Source: UCB CHEMICALS BRUSSELS
Test substance: Fifteen Sprague Dawley rats/sex/group were administered Thiram technical (98.8 % purity) in the diet at concentrations of 0, 30, 125 and 500 ppm. Animals were treated over a period of at least 90 days and euthanized during the fourteenth week of administration.
Reliability: (1) Valid without restriction

(96)

Type: Neurotoxicity
Remark: Type : Neurotoxicity (90-day study)

Results :

Mortality : no incidence

500 ppm : body weight and fgood consumption depressed. Neurotoxicity findings (through F0B, motor activity, neuropathology) : no consistent evidence of neurotoxicity shown overall (however, F0B affected slightly).
125 ppm : adverse effects on body weight, food consumption.

However, less severe than with 500 ppm.
Neurotoxicity : no findings noted.
30 ppm : no toxic effects any kind.
NOEL : (neurotoxicity) : 125 ppm.
NOEL : (adult toxicity) : 30 ppm.
Method : EPA/FIFRA par. 82-5
Year : 1991
GLP : yes

Source: UCB-Chemicals Gent

Test substance: Fifteen Sprague Dawley rats/sex/group were administered Thiram technical (98.8% purity) in the diet at concentrations of 0, 30, 125 and 500 ppm. Animals were treated over a period of al least 90 days and euthanized during the fourteenth week of administration.

Reliability: (1) Valid without restriction

(97)

Type: Toxicokinetics

Remark: The identification of thiram metabolites in urine was determined in 2 Charles River Crl : CDr(SD)BR rats/sex. The rats (approximately 5 weeks old) were fed diets containing 50 ppm unlabelled thiram for nine weeks followed by a single oral dose of 14c-thiram (purity 99 %). Samples of urine were collected over the first 24 hours after treatment termination and analyzed by HPLC.

Approximately 60 % of the administered radioactivity was recovered as expired CS2 and 30 % was found in the urine. Thiram was rapidly degraded to more polar products. Virtually no unchanged thiram was detected in the urine. Five urinary metabolites were detected by HPLC and were identified by mass spectrometry. The identified metabolites were an alanine derivative of CS2 (10 %); a glucuronide conjugate of dimethyldithiocarbamate (DDC) (20 %); a thiosulfenic acid (34 %); the methyl ester of DDC (6%); and an alanine conjugate (30 %). The presence of these polar conjugates demonstrates that the metabolic pathway involved a reduction of the disulphide bond and subsequent reactions of the thiol moiety to form oxidative and conjugative polar products.

Source: UCB CHEMICALS BRUSSELS

Reliability: (1) valid without restriction

(98)

Type: Toxicokinetics

Remark: The identification of thiram metabolites in urine was determined in 2 Charles River Crl : CDr(SD)BR rats/sex. The rats (approximately 5 weeks old) were fed diets containing 50 ppm unlabelled thiram for nine weeks followed by a singleoral dose of 14C-thiram (purity 99%).
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conjugates demonstrates that the metabolic pathway involved a reduction of the disulphide bond and subsequent reactions of the thiol moiety to form oxidative and conjugative polar products.

Source: UCB-Chemicals Gent
Reliability: (1) Valid without restriction

(99)

Type: Other
Remark: Increased number of abnormal sperm have been reported in mice given TMTD at 50 or 100 mg/kg ip. or 80, 200 or 320 mg/kg orally in three daily doses for ????? days.
Zdzienicka, M. et al (1982). Thiram induced sperm-head abnormalities in mice. Mutat. Res. 102, 261.
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Source: Akzo Nobel Chemicals GmbH Dueren
Reliability: (4) Unassignable – data from secondary literature sources

5.11 Experience with Human Exposure

Remark: Alcohol intolerance may result from exposure to dithiocarbamates.
Source: Akzo Nobel Chemicals GmbH Dueren

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Halflife: 17.2 days for the 11 day study
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